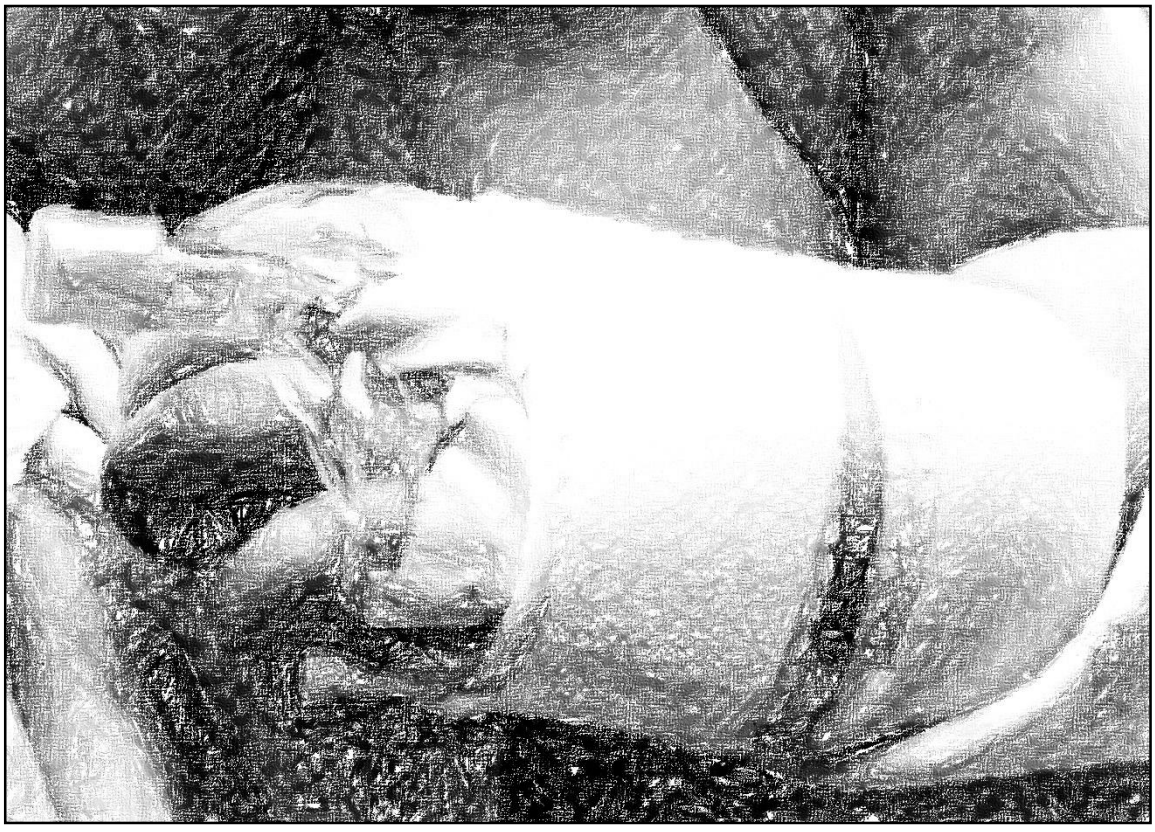
Department of Paediatrics & Child Health

UNIVERSITY OF CAPE TOWN

ANNUAL RESEARCH DAYS 2017



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Programme and Abstract Book

31st October & 01st November
D3 Lecture Theatre, D Floor
Red Cross War Memorial Children's Hospital

CPD Points for Tuesday, 31 October 2017 and Wednesday, 01 November 2017

Please sign the attendance register on both days to claim your points.

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Abstract of Keynote Address

Title: **RESEARCH: LESSONS FROM RISKY BUSINESS**

Keynote Speaker: AC Argent

Introduction
In the world of clinical medicine there are unfortunately multiple points at which things can go wrong. Research and particularly clinical research similarly has high intrinsic risks and it may be useful to consider aspects of the research process that could be improved using approaches and insights that have come from the experience of people who work in high risk environments.

The context
Processes can be categorized in many ways including: simple, complicated and complex processes. Simple processes are just that, but to get them right all the time requires constant care (e.g. hand hygiene); complicated processes require time, attention to detail, but as long as the process is completed appropriately the results are predictable. Complex processes are those where the consequences of changes are not entirely (or at all) predictable and unfortunately clinical and clinical research often fall into this category with the consequence that one constantly needs to evaluate the effects of changes (which might appear insignificant initially).

Virtually all research happens in the context where there is a tension between the resources available for the research; the pressures to get the research done (and often to get clinical and other duties completed) and the risks of things going wrong (alternatively the safety of the process). Sometimes it is possible to avoid adverse events in this context by the establishment of very structured processes which are operated by personnel with very high levels of training and expertise. Overall there is a constant need for review of the tensions in this relationship

Approaches that might help

Development of a deep understanding of processes
One of the challenges of applying for grants, of getting funding for research is that often the application process calls for broad sweeps and conceptual frameworks. By contrast the process of much research requires constant focus on the minutiae of getting every detail correct.

Getting the planning right
While there are many systems that can be optimized by constant improvement, it saves vast amounts of resources if in fact the planning can be exactly right from the very beginning. There is increasing recognition that processes such as simulation may be remarkably useful in taking abstract ideas into very practical reality.

Constant streamlining
Importantly there are fields of research where actually the detailed minutiae may not be that important. In some areas of quality-improvement research it may be appropriate to collect the minimum detail required so as to make sure that overall trends can be identified in a way that is pragmatic and realistic?

The challenge is being able to identify the value added by each process, and the quality of data that is required at each point. Ideally each step in a system should add significant value and take as little time as possible.

Constant attention to quality improvement (by each person in the process)
The Lean systems are one aspect of processes where managers have focused on development of cultures and processes of constant improvement. In these systems there is a perception that constant improvement is required, but that the people most able to bring about that improvement are actually those who work "on the shopfloor". Constant involvement of research personnel in this sort of process has significant potential to improve the quality of research processes.

Importantly these approaches insist that the "system" should be consistently improved, and that "work-arounds" are actually not the answer to problematic processes.

Understanding of human factors
Human factors, broadly refer to all the aspects that humans bring into any enterprise. A deeper understanding of how human behavior (both individually and as groups) affects the processes and quality of research projects has the potential to substantially improve outcomes from research

Creating a "learning environment"
In learning environments, there is both the recognition that mistakes and errors will occur, and the capacity to learn from those events. Initially that requires that people are encouraged to report and admit to adverse events in a non-punitive environment. Establishing processes that enable lessons to be learnt from adverse events may be even more challenging.

We often focus on adverse events in attempts to bring about improvement, but there is also the potential to focus on processes and events that work really well and to understand the keys features of those.

Developing resilience
An inherent requirement of high functioning and reliable systems is that they are able to adapt rapidly and effectively to change. In addition resilient systems are able to deal with unexpected events in creative and positive ways.

Conclusions
In many senses research is a "high risk enterprise", where projects may fail to achieve the required results or suffer significant complications. Part of the research process could perhaps focus on how we can optimize many aspects of research and produce fewer "errors" and more data that can actually be integrated into clinical practice

Title: **CHALLENGING BELIEFS: CHANGES IN GMFCS TWO DECADES AFTER SELECTIVE DORSAL RHIZOTOMY OR ORTHOPAEDIC SURGERY**

Authors: Nelleke G. Langerak[1], A. Graham Fieggen[1], Robert P. Lamberts[2]

Affiliation: [1]Division of Neurosurgery, University of CapeTown, Cape Town, South Africa
[2]Division of Orthopaedic surgery, Stellenbosch University, Cape Town, South Africa,

Objective:
The Gross Motor Function Classification System (GMFCS) is a well-accepted tool to objectively classify the level of gross motor function in people with Cerebral Palsy (CP) [1]. While the GMFCS has been shown to be stable [2,3], it is not known whether major interventions lead to long term changes in GMFCS level. The aim of this study was to determine in adults with bilateral spastic CP whether there was i) a change in GMFCS level two decades following a major intervention, either Selective Dorsal Rhizotomy (SDR) or Orthopaedic surgery (ORTH); and ii) a relation between change in GMFCS levels and contextual factors such as age, sex, education, employment, marital and socioeconomic status.

Methods:
Participants were recruited from databases of a children's hospital and a special needs school in Cape Town, South Africa. Pre-operative GMFCS levels were retrospectively determined from clinical records while current GMFCS levels and information on contextual factors was captured at the time of follow-up assessment. The study cohort consisted of 61 participants, including 31 in SDR group (mean (SD) age: 28y8m (5y6mo), 13 females) and 30 in ORTH group (age: 33y1mo (7y8mo), 18 females). Statistical analyses included Wilcoxon matched-pairs signed rank tests (aim i) and Spearman correlations (aim ii).

Results:
Preoperatively, 9 children could be classified as GMFCS level I (0-SDR, 9-ORTH), 36 as level II (22-SDR, 14-ORTH) and 16 as level III (9-SDR, 7-ORTH), while after a mean (SD) follow-up time of 24y3mo (6y2mo) 30 participants were classified as level I (15 SDR, 15 ORTH), 22 as level II (11-SDR, 11-ORTH), and 9 as level III (5-SDR, 4-ORTH). Of the 33 participants for whom the GMFCS level changed, 30 improved at least one level (18-SDR, 12-ORTH) and 3 deteriorated one level (0-SDR, 3-ORTH), while 28 (13-SDR, 15-ORTH) were unchanged. The changes in GMFCS level were significant (All: $p<0.0001$; SDR: $p<0.0001$; ORTH: $p=0.04$) and only associated with pre-operative GMFCS levels (All: $p=0.04$, $r=0.26$; ORTH: $p<0.01$, $r=0.48$).

Conclusions:
Two decades after SDR or orthopaedic surgery, more than half of this study cohort was classified at a different GMFCS level compared with pre-operative levels, with the majority experiencing an improvement. These findings suggests that in some circumstances (e.g. in developing countries) GMFCS can change after major interventions.

[1] Palisano et al. DMCN 2008;50:744–50.
[2] Palisano et al. DMCN 2006;48:424–28.
[3] Alriksson-Schmidt et al. DMCN 2017;59:641-646.

HREC nr: SDR study (UCT): REC REF 139/2005; ORTH study (SUN): N10/05/181

Title: **EXAMINING CEREBRAL METABOLISM USING MICRODIALYSIS IN CHILDREN WITH SEVERE TRAUMATIC BRAIN INJURY**

Authors: Ursula Rohlwink, Nico Enslin, Jacob Hoffman, Sinead Ross, Graham Fieggen, Anthony Figaji

Affiliation: Division of Neurosurgery, University of Cape Town, South Africa

Objectives:
Outcomes after severe traumatic brain injury (TBI) in children can be improved by reducing secondary injury but these mechanisms are poorly understood. Brain microdialysis is an advanced technique with clinical and research potential that is largely unexplored in children. In a pediatric TBI cohort we used microdialysis to examine brain metabolism in association with outcome and other indicators of brain physiology.

Methods:
Cerebral metabolite data were analysed in children with severe TBI (GCS≤8) who had multimodality monitoring including microdialysis, brain tissue oxygen tension ($PbtO_2$) and intracranial pressure (ICP). Brain extracellular fluid (ECF) samples were collected hourly from the microdialysis catheter for a maximum of 5 days and were analysed at the bedside (Iscus Flex, MDialysis) for metabolites (lactate, pyruvate, lactate/pyruvate ratio [LPR], glucose, glycerol, glutamate). ICP, $PbtO_2$ and cerebral perfusion pressure (CPP) data were collected continuously and averaged for comparison. Systemic glucose was recorded from arterial blood gases.

Results:
We analysed metabolite data in 22 patients (median age 7 [0.4-13] years). High brain LPR was associated with low $PbtO_2$ (correlation $r=-0.6$, $p<0.01$, AUC 0.9 for $PbtO_2$ <10mmHg) and high ICP ($r=0.35$, $p<0.01$). An elevated LPR (≥40) was associated with increased mortality ($p<0.01$) and poor clinical outcome ($p=0.02$). ECF glucose decreased at lower CPPs in keeping with a lower limit of autoregulation, but was only moderately correlated with systemic glucose ($r=0.4$, $p<0.01$). Glycerol increased with contusions and demonstrated dynamic trends consistent with cellular injury.

Conclusion:
This is the first comprehensive set of microdialysis data for children. It is a promising real-time clinical tool to examine dynamic brain chemistry changes associated with secondary injury, and may help to better understand the complex pathophysiology of TBI, generate new questions, and direct treatment strategies.

Ethics number: HREC 060/2011
Not previously presented at Paediatrics and Child Health research days

Title: **DIFFERENT WHITE MATTER ABNORMALITIES IN CHILDREN WITH SPASTIC DIPLEGIA DUE TO HIV ENCEPHALOPATHY VERSUS CEREBRAL PALSY**

Authors: Jia Fan[1], Kirsten A Donald[2], Ernesta M. Meintjes[1], Tracy Kilborn[3], Theresa N. Mann[4], A. Graham Fieggen[5], Robert P. Lamberts[4], Nelleke G. Langerak[5]

Affiliation: [1]MRC/UCT Medical Imaging Research Unit, Department of Human Biology, University of Cape Town, Cape Town, South Africa, [2]Pediatrics and Child Health, Red Cross War Memorial Children's Hospital, University of Cape Town, Cape Town, South Africa, [3]Pediatric Radiology, Red Cross War Memorial Children's Hospital University of Cape Town, Cape Town, South Africa, [4]Orthopaedic surgery, Stellenbosch University, Cape Town, South Africa, [5]Neurosurgery, University of Cape Town, Cape Town, South Africa

Objective:
Human immunodeficiency virus (HIV) impacts on the central nervous system (CNS) in infected individuals. HIV encephalopathy (HIVE) is one of the most common primary HIV-related CNS diseases resulting in neurologic dysfunction. Cerebral palsy (CP) refers to a group of permanent but non-progressive movement disorders that occurred in the developing fetal or infant brain. It has previously been reported that the gait pattern of children with HIVE showed similarities to spastic diplegic CP, including stiff knee gait and equinus ankle. However, brain abnormalities caused by HIVE may be different to those caused by CP due to their different etiologies. Therefore, the first aim of the study was to examine white matter (WM) differences between children with HIVE and children with CP using diffusion tensor imaging (DTI), a neuroimaging technique providing information on the microstructural integrity of fibre pathways connecting distinct brain regions, which has not been specifically studied in children with HIVE. There is increasing interest in correlations between tract damage and gait parameters. This information may hold prognostic value, and guide specific early therapy.

Methods:
Participants were recruited from hospitals and special needs schools in Cape Town and included 27 children with HIVE (mean age: 8.7±2.2 years, 11 boys) and 14 with CP (mean age: 8.7±2.1 years, 9 boys). Each child was scanned on a 1.5 T Phillips scanner located at Red Cross War Memorial Children's Hospital. DTI and T1-weighted structural images were obtained. All DTI data were preprocessed using TORTISE. The relevant maps of DTI scalar parameters, fractional anisotropy (FA) and mean diffusivity (MD), were generated and coregistered to an Magnetic resonance imaging (MNI) pediatric standard image using linear and nonlinear coregistration algorithms. A threshold at FA>0.2 was applied to ensure that only WM was included. Voxelwise comparisons were performed to identify regions showing group differences, and we only reported the results that survived cluster size threshold at $p<0.01$. Gait patterns, sagital plane knee flexion/extension ROM and maximum ankle dorsiflexion parameters, were recorded using three-dimensional gait analyses (3DGA) and correlated to the mean DTI parameters extracted in each cluster showing group difference using Pearson's correlation.

Results:
Voxelwise analyses revealed lower FA and higher MD in children with HIVE within the right (R) corticospinal tract (CST) compared to children with CP. Conversely, reduced FA and increased MD were seen in children with CP compared to children with HIVE in 3 regions—R anterior thalamic radiation (ATR), body of corpus callosum (BCC) and splenium of corpus callosum (SCC). Children with CP also showed higher MD in left (L) ATR and L superior longitudinal fasciculus (SLF). No significant association was found between DTI parameters and gait parameters in the HIVE-derived clusters. However, the mean FA in the BCC was significantly related with both knee flexion/extension ROM ($r=0.79$; $p=0.001$) and ankle maximum dorsiflexion ($r=0.67$; $p=0.009$) in the CP-derived clusters.

Conclusions:
This study provides evidence of WM microstructural abnormalities in the CST of children with HIVE. The CST is involved in motor control function and may relate to the typical spastic diplegic gait pattern. These findings are consistent with a previously reported study which showed WM deficits in the CST in children with HIV (but not necessarily HIVE) compared to healthy controls. On the other hand, the children with CP revealed WM abnormalities in ATR, BCC, SLF and SCC compared to children with HIVE. These findings suggests that the HIV virus may play a direct role in the etiology of this severe physical neurological manifestation of HIVE and that the underlying neurobiological basis of the abnormal neurological findings of the two conditions are different despite their similar clinical phenotype at face value.

Title: **EARLIER TREATMENT AND LOWER MORTALITY IN INFANTS INITIATING ANTIRETROVIRAL THERAPY AT < 12 WEEKS OF AGE IN SOUTH AFRICA - THE INTERNATIONAL EPIDEMIOLOGIC DATABASES TO EVALUATE AIDS SOUTHERN AFRICA (IeDEA-SA) COLLABORATION**

Authors: Victoria Iyun, Karl Technau, Brian Eley, Helena Rabie, Andrew Boulle, Geoff Fatti, Frank Tanser, Robin Wood, Lee Fairlie, Mary-Ann Davies

Background:
The context of HIV prevention and treatment for children in South Africa has significantly improved and there is a recent shift toward birth early infant diagnosis and early infant antiretroviral therapy (ART). We described the characteristic and outcomes of children initiating ART in the context of changing paediatric HIV testing and treatment guidelines in South Africa.

Methods:
A retrospective cohort analysis was conducted using data from the IeDEA-SA collaboration. HIV-infected infants initiating combination ART at <3 months old in South Africa, from 2006-2016 were included. We described changes in characteristics of infants starting ART as well as mortality, loss to follow-up (LTFU) and transfer out by 6 months on ART.

Results:
Among 1380 infants, the median age at ART initiation was 56 days (interquartile range (IQR) 27-73); median time on ART was 13.6 months (IQR4.0-34.5). The median age at ART start decreased from 61 days (IQR 46-75) in 2006-2009 to 34 days (IQR 1-66) in 2013+ ($p<0.001$). There was a moderate decline in median log viral load at ART initiation from 5.9 (IQR 5.4- 6.4) in 2006-2009 to 5.4 (IQR 3.9-6.3) in 2013+ ($p<0.001$). The median absolute CD4 count (cells/μL) increased progressively from 888 (IQR 380-1703) in 2006-2009 to 1526 (IQR 659-2231) in 2013+ ($p<0.001$). Among infants with data on WHO disease staging (n=865), 84% (n=299) started ART with WHO disease stage 3/4 in 2006-2009 compared to 39% (n=279) in 2013+ ($p<0.001$). After 6 months on ART, 10% (median age 68 days (IQR 55-75)) and 5% (median age 60 days (IQR 25-83)) of children died in 2006-2009 and 2013+ respectively ($p<0.001$). LTFU decreased from 22% in 2006-2009 to 14% in 2013+ ($p=0.004$) and transfer out declined from 20% in 2006-2009 to 12% in 2013+ ($p<0.001$).

Conclusions:
Children are starting ART earlier, with less progressive disease and associated declines in mortality; however mortality and LTFU in infants starting ART remains unacceptably high. In view of the scale up of birth PCR testing in South Africa, a significant proportion of children still start ART with advanced disease, highlighting the need for a focused approach to early infant HIV testing and follow-up on ART.

Title: **AN ASSESSMENT OF THE ISONIAZID PREVENTIVE THERAPY PROGRAMME FOR CHILDREN IN A BUSY PRIMARY HEALTHCARE CLINIC IN NELSON MANDELA BAY HEALTH DISTRICT, EASTERN CAPE PROVINCE**

Presenter: Jawaya Shea (obo Faye Tucker)

Introduction:
Tuberculosis (TB) is a significant contributor to the international and national burden of disease. Global estimates suggest that there were 10.4 million new cases of TB in 2015. Children account for approximately 10% of these cases although in South Africa this figure is thought to be higher. Despite clear evidence that Isoniazid preventive therapy (IPT) can reduce the risk of progression from TB infection to disease in TB contacts, IPT has been poorly implemented in South African national TB control programmes.

Objectives:
To determine current practices regarding the identification and management of child contacts (<5 years of age) at a primary care clinic in the Nelson Mandela Bay Health District, Eastern Cape Province.

Methodology:
A cross-sectional descriptive study was conducted using a retrospective record review from infectious TB index patients aged ≥15 years. Folders of index patients with bacteriologically confirmed pulmonary TB, who started TB treatment between 21 October 2011 and 28 February 2014, were included. A sample size of 246 child contacts was required to obtain adequate power. A 95% confidence level was used to determine statistically significant results.

Results:
491 index patient records were assessed and 261 child contacts identified. 87.5% (n=430) of index patient folders had contacts documented although only 0.53 child contacts were identified per index patient. Of the 261 child contacts identified, 184 (70.5%) were screened for TB, two were started on TB treatment and 108/184 (58.7%) were initiated on IPT. The remaining 74 (40.2%) children had no documentation of further management. Only four (3.7%) children completed the 24 week IPT course. Male patients reported fewer child contacts (Chi-squared=7.31; p=0.01; OR=0.6; 95%CI=0.42-0.86) and were less likely to bring contacts for screening (Chi-squared=8.98; p=0.003; OR=0.41; 95%CI=0.24-0.72), Re-treatment index patients were also less likely to bring contacts for screening (Chi-squared=6.37; p=0.01; OR=0.45, 95%CI=0.25-0.81) and those that were screened were less likely to initiate IPT (Chi-squared=4.05; p=0.04; OR=0.54; 95% CI=0.3-0.95).

Conclusion and recommendations:
Despite contacts being well documented, child contacts were poorly identified. The fall-out of children at each step from identification to IPT completion was unacceptably high. Contacts of male and retreatment index patients are at greater risk of poor management. Recommendations to improve IPT delivery at national and local level include a review of the national IPT guidelines considering the relative success of shorter courses of TB prophylaxis, the use of standardised IPT stationary, staff training and the involvement of community health workers in contact management.

Title: **PREVALENCE OF MICROALBUMINURIA IN PERINATALLY HIV-INFECTED ADOLESCENTS ON ANTIRETROVIRAL THERAPY**

Authors: Lisa Frigati, Sana Mahtab, Peter Nourse, Patricio Ray, Sofia Perazzo, Takwanisa Machemedze, Nana Akua Asafu-Agyei, Landon Myer, Heather Zar

Background:
Use of antiretroviral therapy (ART) has changed the pattern of renal disease in HIV-infected children from predominantly glomerular injury to tubular dysfunction. There is however relatively little data on the prevalence and course of renal disease in perinatally HIV -infected adolescents (PHIVA) in Africa in the era of ART and a lack of surveillance for HIV-associated kidney disease.

Objective:
To assess the prevalence of proteinuria or microalbuminuria in South African PHIVA stable on ART and age-matched HIV- uninfected adolescents

Methods:
511 PHIVA and 109 age-matched controls enrolled in the Cape Town Antiretroviral Adolescent Cohort (CTAAC) were included. Inclusion criteria for PHIVA were ages 9-14 years, on ART for at least 6 months and resident in Cape Town, South Africa**.** A structured clinical interview and examination including blood pressure and anthropometry was done; blood (for urea and creatinine) and urine was collected. Urine dipstix was done for proteinuria and the remainder of the urine was stored in 3 aliquots at -80° C, batched and sent for testing for microalbuminuria (Albumin Creatinine ratio, ACR >30mg/g).

Results:
Amongst PHIVA (50% female), the median age was 12.0 (IQR: 10.7-13.3) and 11.8 (IQR: 10.1-13.4) in HIV-uninfected adolescents. 473 (92.6%) of PHIVA and all controls were Black African. In PHIVA, median duration of ART was 7.6 years (IQR: 4.6-9.3) with only 7 adolescents on a Tenofovir containing regimen at time of enrollment visit. 188 (37.3%) were on a protease inhibitor regimen although none were on Indinavir. 425 (83.2%) had a CD4 count > 500 cells/ mm^3 and 391 (76.7%) had a viral load of less than 50 copies/ml.

The prevalence of any proteinuria (trace – 3+) or microalbuminuria was 6.6% and 8.5% respectively, which was similar in HIV-infected and uninfected adolescents. Median blood pressure (both systolic and diastolic) was higher in PHIVA than in HIV-uninfected adolescents (105 vs 108 and 67 vs 69, p=0.00 and 0.04) but this is unlikely to be clinically significant.

Conclusions:
Proteinuriua or microalbuminuria were uncommon in this cohort of well controlled PHIVA, with similar prevalence in PHIVA and HIV-uninfected adolescents. Assessing for microalbuminuria may allow identification of adolescents at risk of HIVAN to implement more intensive follow up. Follow up of participants with microalbuminuria may inform long term outcomes and potential strategies for screening and management of this growing population of HIV-infected youth.

Funding: NIH R01HD074051

Ethics: 051/2013

Title: **TREATMENT OUTCOMES IN PERINATALLY-HIV-INFECTED CHILDREN AND ADOLESCENTS AFTER 10 YEARS ON ANTIRETROVIRAL THERAPY**

Authors: Kim Anderson, Rudzani Muloiwa, Mary-Ann Davies

Objective:
The burden of paediatric HIV infection in South Africa has shifted to older children and adolescents, owing to improvements in prevention of new vertical infections and the success of paediatric antiretroviral therapy (ART) programmes that increase life-expectancy in perinatally-HIV(PHIV)-infected children. Nevertheless, information on long-term treatment outcomes in this unique group of highly treatment-experienced adolescents in the local setting is very limited. We aimed to examine the long-term immunologic and virologic outcomes of ART in children who remain in care for at least 10 years.

Methods:
We included PHIV-infected children who initiated ART at Groote Schuur Hospital, Cape Town, between 2002 and 2005, and had follow-up at the clinic for a minimum of 10 years from ART initiation date. Clinical data was extracted by folder review and laboratory data was extracted from the National Health Laboratory Service database. Anthropometric measurements, CD4 counts and viral loads (VLs) were analysed for each successive year on ART.

Results:
The median follow-up among 127 patients included was 12.2 years (IQR 11.1 – 13.0). At ART initiation, the median age was 2.6 years (IQR 1.3 – 4.9) and the mean CD4 percentage was 13.7% (95% CI 13.6 – 13.9). The proportion with HAZ, WAZ and BAZ <-2 were 72.6%, 49.6% and 13.3% respectively.
The first ART regimen was NNRTI-based in 64% of children and PI-based in the remaining 36%.
After 10 years since initiating ART, 49.6% (n=63) of patients were on 1st-line ART, 43.3% (n=55) on 2nd-line ART, 3.1% (n=4) on lamivudine monotherapy and 3.9% (n=5) on no ART. The proportion with HAZ and BAZ <-2 were 32.7% and 7.1% respectively.
After 10 years since initiating ART, 87.5% had CD4 >500 cells/µl (98% of those on 1st-line vs 79% of those on 2nd-line ART; p=0.003). In those who had VL performed after 10 years, 74.3% (81/109) had VL <400 copies/ml (81.5% of those on 1st-line vs 69.2% on 2nd-line ART; p=0.16). The percentages of patients with viral suppression and optimal immune status at each year since ART initiation showed a declining trend in the adolescent years.
The 10-year probability of experiencing viral failure (VF) was 56.7% (95% CI 48.3 – 65.5) with median time to VF of 5.2 years (95% CI 2.0 – 10.2). Children on NNRTI-based regimens had a higher 10-year probability of VF (65.8%) compared to those on a PI-based regimen (43.1%; logrank test, p=0.04). The 10 year probability of switching to 2nd-line ART was 45.7% (95% CI 37.5 -54.8).

Conclusions:
After 10 years on ART, 74% of PHIV-infected adolescents were virally suppressed and 88% had optimal immune status. The proportion of children who were stunted was 33%. The 10 year probability of experiencing VF was 57%. Virologic and immunologic outcomes were good overall, but 43% of adolescents were on 2nd-line ART with poorer immunologic outcomes, and a trend was observed of declining optimal virologic and immunologic outcomes in the adolescent years.

Acknowledgements:
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HREC Ref: 891/2015

Title: **WHAT SHOULD WE DO WHEN HIV-POSITIVE CHILDREN FAIL FIRST-LINE COMBINATION ANTI-RETROVIRAL THERAPY (cART)? – A COMPARISON OF 4 ART MANAGEMENT STRATEGIES**

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Objective:
Virologic failure (VF) in HIV-infected children is difficult to manage in resource-limited settings, given limited availability of alternative drugs and concerns around adherence and development of viral resistance. We aimed to evaluate four management strategies for children following their first episode of VF by comparing their immunologic and virologic outcomes.

Methods:
Children (age <16 years at cART start) with VF, defined as having ≥2 consecutive unsuppressed viral loads (>1000 copies/ml) ≥1 month apart after ≥6 months on cART (at least 3 anti-retroviral drugs from at least 2 drug classes), were followed from their first episode of VF, starting from their second unsuppressed viral load (VL). Children from 8 IeDEA-SA cohorts initiating ART between 2004-2010, with recorded CD4% at VF, and with ≥1 subsequent CD4% were included. Children with VF followed one of four management strategies: 1) Continuing on their failing regimen with at most 1 same-class drug substitution; 2) Switching to a new cART regimen based on guidelines or resistance testing; 3) Switching to a holding regimen, either lamivudine monotherapy or other non-cART regimen; 4) Discontinuing all anti-retrovirals. We compared the effect of management strategy choice, relative to strategy 1, on both the 52-week change in CD4% and $\log_{10}$VL from VF, using the inverse probability weighting of a marginal structural linear model.

Results:
We included 982 patients (584 and 398 on non-nucleoside reverse transcriptase inhibitor [NNRTI] and protease inhibitor-based regimens respectively) with 54168 weeks of follow-up, of which 73.5% was spent on strategy 1, 23.8% on strategy 2, 1.0% on strategy 3 and 1.8% on strategy 4. All patients started on strategy 1, 564 remained on strategy 1, 328, 25 and 65 switched to strategies 2, 3 and 4 respectively. Relative to strategy 1, those switched to strategy 2 had a predicted gain in CD4% of 1.5% (95% CI 0.1-2.7) and a decline in $\log_{10}$VL of -1.4 (95% CI -2.0, -0.8) 52 weeks after VF, whereas those switched to strategy 3 or strategy 4 had predicted declines in CD4% of -4.5% (95% CI -10.0, 1.0) and -5.0% (95% CI -14.3, 4.3) respectively, and predicted gains in $\log_{10}$VL of 0.2 (95% CI -3.6, 4.1) and 0.8 (95% CI -0.6, 2.1). When restricting to those on NNRTI-based first-line, we found similar CD4% outcomes in those switching to strategy 2 (1.3%, 95% CI 0.1, 2.5) or 3 (-5.9%, 95% CI -12.8, 1.0), but larger declines for those switched to strategy 4 (-18.0%, 95% CI -33.4, -2.7). Viral load outcomes were similar to the main analysis for all three strategies: strategy 2: -1.4, (95% CI -2.1, -0.8), strategy 3: 0.5, (95% CI -2.5, 3.5), strategy 4: -0.8, (95% CI -2.9, 1.4).

Conclusions:
Switching to a new cART regimen resulted in improved immunologic and virologic outcomes when compared with remaining on a failing regimen, whilst switching to a holding regimen or interrupting treatment showed declines in immune response compared to staying on a failing first-line regimen. The results provide useful guidance for the management of children failing treatment, especially those on NNRTI-based regimens.

Title: **DEVELOPMENTAL OUTCOMES OF BREASTFED, HIV-EXPOSED UNINFECTED AND BREASTFED, HIV-UNEXPOSED CHILDREN IN THE CONTEXT OF UNIVERSAL MATERNAL ANTIRETROVIRAL THERAPY: A PROSPECTIVE COHORT**

Authors: Stanzi M le Roux [1], Kirsty Donald [2,3], Kirsty Brittain [1,4], Tamsin K Phillips [1,4], Allison Zerbe [5], Kelly K Nguyen [1,4], Max Kroon [2], Elaine J Abrams [5,6], Landon Myer [1,4]

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Background:
Perinatal exposure to maternal HIV and triple-drug antiretroviral therapy (ART) may impact early childhood development. However, little is known about the developmental outcomes of breastfed, HIV-exposed uninfected children (HEU) born under current recommendations of universal, lifelong maternal ART, and few studies have included appropriate HIV-unexposed (HU) comparators.

Objective:
We examined developmental outcomes among breastfed HEU and HU children from a peri-urban community in Cape Town, South Africa.

Methods:
HIV-infected (HIV+) women initiating universal, lifelong ART (efavirenz-emtricitabine-tenofovir) under "Option B+" policies, and a comparison group of HIV-uninfected (HIV-) women were enrolled during pregnancy and followed through delivery; breastfeeding mother-infant pairs were then followed for up to 18 months postpartum. Developmental assessments were conducted at approximately 12 months of age with Bayley Scales of Infant Development (BSID-III) excluding those with HIV-infection, congenital defects, severe cerebral palsy or born at <28 weeks gestation. BSID-III composite cognitive, motor and language scores (mean 100, SD 15) were categorized to indicate "some" (<85) and "no" (≥85) delay. Potential third variables included preterm birth (<37 weeks); small-for-gestational-age (SGA, birthweight<10th centile); gender; breastfeeding duration and maternal psycho-social/economic factors including intimate partner violence (IPV) and risky drinking, measured during pregnancy with standardized tools; logistic regression analysis was used to adjust for confounders.

Results:
Assessments were completed on 521 children (HEU, n=215; HU, n=306), median age 13 months (interquartile range, IQR 12-14). Compared to HIV- women, HIV+ women (pre-ART median CD4 cell count 346 cells/mm^3) had lower levels of secondary education (27% vs 46%, p<0001) and employment (38% vs 47%, p=0.03); breastfed for shorter (median 6 vs. 10 months, p=0.0004) and were more likely to report risky drinking (12% vs <1%, p<0.0001) and IPV (20% vs 8%, p<0.0001). Prevalence of prematurity was similar (HEU, 13% vs. HU, 9%; p=0.31). Compared to HU, a larger proportion of HEU demonstrated delay in cognitive [10% vs. 5%; odds ratio (OR) 2.28, 95% CI 1.13-4.60] and motor domains (9% vs 5%; OR 2.10, 95% CI 1.03-4.28), but not language (18% vs. 14%; OR 1.28, 95% CI 0.80-2.05). There was evidence of interaction between HIV-exposure and prematurity on motor delay (p=0.03). Compared to term HU, term HEU did not have increased odds of motor delay (OR 1.56, 95%CI 0.64-3.82); preterm HU had 4-fold higher odds of delay (OR 4.47, 95% CI 1.30-15.32), with highest odds of delay among preterm HEU (vs. term HU, OR 14.19, 95% CI 5.09-39.56). Associations persisted after adjusting for gender, maternal age, education, employment, housing, IPV, risky drinking and duration of breastfeeding.

Conclusions:
HEU children demonstrated higher risk of cognitive and motor delay compared to HU children, even in the context of universal maternal ART and breastfeeding. Those born both preterm and HEU appear to be at particularly high risk for delay, a novel finding which warrants further investigation.

HREC Ref: 650/2015

This research has been presented at the following events:

1. 9th Pediatrics HIV workshop in Paris, France: 22 July 2017
2. School of Public Health & Family Medicine Annual research day 2017: 17 August 2017

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Title: **RISK OF VIROLOGICAL FAILURE IN A COHORT OF HIV-INFECTED ADOLESCENTS ON HAART**

Presenter: Rebecca Sher

Background:
Since 2005, global deaths from AIDS have fallen by almost 40% across all age groups except adolescents. In this group, despite the massive upscaling of antiretroviral therapy (ART), AIDS deaths are increasing, making AIDS the leading cause of adolescent deaths in Africa, and the second worldwide. There is a lack of adolescent-specific data, and poor understanding of the way that adherence changes over time.

Our study aimed to describe the risk of detectable viral load in a cohort of HIV positive adolescents on HAART.

Methods:
We conducted a retrospective cohort study of all patients aged 10 - 19 years who attended the HIV Clinic at Groote Schuur Hospital for at least 24 months.

Results:
296 patients met entry criteria, 155 (52,4%) were male. Most of the adolescent were vertically infected (n= 285; 96.3%), with 8 (2.7%) horizontal infections and 3 (1%) unknown mode of infection. Median age of entry into adolescent clinic was 10.4 (IQR 10.0 - 12.8) years and exit age media 17.1 (14.9-19.2) years. Overall, 82 (27.7%) had detectable viral load at entry. The average follow-up period was 5.4 yeas (SD 2.1) for a total follow-up period of 1604 person years. Overall, 148 (50%) of subjects experienced virological failure during the follow-up period. The incidence of viological failure was 117 episodes per 100 person years.

Although 140 (47.3%) of the adolescents had lost at least one parent, loss of parents was not associated with having a detectable viral load; p=0.352. The rate of poor school performance was high with 222 (75%) having repeated at least one class.

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Conclusion:
Half of all adolescents on HAART are at high risk for experiencing elevated viral load during their follow-up on what should otherwise be effective treatment.

Title: **ACCURACY OF XPERT MTB/RIF ULTRA FOR THE DIAGNOSIS OF PULMONARY TUBERCULOSIS IN CHILDREN**

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Background:
Rapid microbiologic confirmation of pulmonary TB (PTB) in children is desirable for diagnosis and effective therapy. A meta-analysis reported a pooled sensitivity and specificity for Xpert MTB/Rif (Xpert) on induced sputum (IS) of 62% and 98% respectively, compared to culture in children. Xpert MTB/Rif Ultra (Ultra) can detect disease with fewer bacilli than Xpert and so may offer an improved rapid diagnostic, as childhood PTB is paucibacillary. We investigated the diagnostic yield of Ultra compared to liquid culture from an IS sample in children in a high HIV and TB prevalence area.

Methods:
Children hospitalised for suspected PTB in Cape Town, South Africa were prospectively enrolled from Sep 2012 to Sept 2016. One to three IS were collected; the first was split for culture in liquid medium (mycobacterial growth indicator tube, MGIT) and Xpert; the second was split for culture and Xpert or storage; the third was stored. Ultra was performed in Dec 2016, on a single IS specimen from the batched stored 2nd or 3rd IS specimen. The accuracy of Ultra was compared to culture as the reference standard.

Results:
367 samples with valid culture results were available. The median (25th-75th percentile) age of children was 33.0 (15.2-74.0) months; 71 children (19.4%) were HIV-infected. On per sample analysis, culture was positive in 73 (19.9%) and Ultra in 64 (17.4%). Xpert MTB/Rif, available for 112 samples was positive in 17 (15.2%). The sensitivity and specificity of Ultra on the per sample analysis (culture and Ultra on the same sample) were 75.3% and 96.9% respectively which was similar in HIV-infected (sensitivity 70.6%; specificity 98.1%) and HIV-uninfected children (sensitivity 76.8%; specificity 96.6%). Ultra was positive in 8 children with negative culture results of whom all were clinically diagnosed and treated as 'unconfirmed TB' per NIH revised consensus classification. The sensitivity and specificity of Ultra on a per patient analysis (Ultra from one IS sample compared to culture results from multiple IS samples) were 67.5% and 97.2% respectively. If the 8 clinically diagnosed TB cases with a positive Ultra were assumed to be true positives, the sensitivity and specificity of Ultra on the per sample analysis were 77.8% and 99.7% respectively.

Conclusion:
Ultra provides rapid detection of *M tuberculosis* complex from a single IS in most children with culture confirmed TB. Ultra may detect an additional group of children with TB, who are not detected by culture.

Funding: National Institutes of Health, USA, Medical Research Council, South Africa, TB-REPORT. Ultra cartridges supplied by FIND Diagnostics

Title: **THE SHORT-TERM OUTCOMES OF HIV EXPOSED VS. HIV UNEXPOSED VERY LOW BIRTH WEIGHT INFANTS**

Authors: Linda Riemer, Michael C Harrison, Lloyd Tooke

Introduction:
HIV exposed but uninfected infants have been shown to have a higher morbidity and mortality than unexposed infants. There is almost no literature comparing the short-term outcomes of HIV exposed versus unexposed very low birth weight neonates who are born prematurely.

Aim:
The primary outcome was to evaluate the short-term neonatal outcomes of a cohort of HIV exposed and HIV Unexposed Very Low Birth Weight infants to determine if HIV exposure conveys increased morbidity and mortality risk. Secondary outcomes included evaluation if adequate maternal ARV exposure and neonatal PCR status conveyed any differences in short-term neonatal outcomes.

Methods:
A retrospective review of all neonates ≤1500grams who were admitted at Groote Schuur Hospital nursery between January 2012 and December 2014. Data were obtained from the Vermont Oxford Database and the Prevention of Mother to Child Transmission register.

Results:
A total of 1593 neonates were admitted during the 3 years of which it was possible to obtain maternal HIV status in 1579 babies. Of these 1579 babies, 316 (20%)were HIV exposed. Eleven of the 230 (4.7%)infant Polymerase Chain Reaction tests (PCR) were positive. There was no difference in mortality, birth weight, gestational age, length of stay, sepsis and delivery room outcomes for the HIV exposed, maternal antiretroviral exposed and PCR positive neonates. Differences between HIV exposed and HIV unexposed neonates were noted in an increased risk of necrotising enterocolitis [OR 1.83 (1.2-2.8) and an increased need for ventilation [OR 1.35 (1.01-1.8)]. Maternal antiretroviral exposed neonates developed less necrotising enterocolitis compared with maternal antiretroviral under-exposed neonates with a birth weight under 1000grams appearing to contribute in the development and outcome of necrotising enterocolitis. Differences in PCR positive neonates included less non-invasive ventilation [OR 0.28, (0.08 – 0.98)], more Chronic Lung Disease [OR 5.49 (1.31 – 23)] and more necrotising enterocolitis [OR 4.12, 1.02 – 17.18)].

Conclusion:
This study is the first to compare the short-term outcomes of HIV exposed and HIV unexposed very low birth weight infants and look at maternal antiretroviral exposure. It demonstrated no difference in birth weight, gestational age, mortality or sepsis. Necrotising enterocolitis is increased in the HIV exposed neonates especially if they are under-exposed to maternal antiretrovirals.

Ethics: HREC 603/2015

Title: **THE INFLUENCE OF ANAESTHETIC METHOD ON OUTCOMES OF PRETERM INFANTS DELIVERED BY CAESAREAN SECTION IN A TERTIARY HOSPITAL IN SOUTH AFRICA: A PILOT REVIEW**

Authors: R Stander, L Tooke, AR Horn

Objectives:
Delivery of preterm infants by caesarean section (CS) is associated with an elevated risk for morbidity and mortality due to the associated intra-partum emergencies, fetal distress, maternal medication and early delivery due to maternal illness. However, the influence of the method of anaesthesia on this group is unclear. The objectives of this study were to describe the indications for CS and the types of anaesthesia in a cohort of preterm infants; to identify a uniform subgroup for whom we could compare the need for resuscitation and related short term outcomes in the above subgroup, comparing regional anaesthesia (RA) to general anaesthesia (GA).

Methods:
We carried out a retrospective, descriptive, cohort study at Groote Schuur Hospital, Cape Town, South Africa. Data was collected on infants born between 1 January and 30 Sep 2014. All preterm infants born at 28 – 35 wks gestation, delivered by CS were eligible for inclusion. Infants with missing data for method of anaesthesia and/or indication for CS were excluded. Indications for CS and type of anaesthesia were obtained from the theatre register. The largest group of infants with similar indications for delivery were identified from the theatre register. Baseline characteristics and short term outcomes for this group were extracted from an existing prospective data base of all infants ≤ 1500g who are born at Groote Schuur Hospital (GSH) (The data base is collected as part of the international Vermont Oxford Data Base). The characteristics and outcomes of infants delivered by RA were compared with those delivered by GA

Results:
There were a total of 249 caesarean sections for preterm infants; data on mode of anaesthesia or indication for CS were missing in 23 infants. Of the remaining 226 preterm caesarean sections; 56 (24%) were delivered via GA and the majority 170 (75%) were delivered under RA. Abnormal CTG, was the commonest indication for CS irrespective of mode of anaesthesia, occurring in 150 (66%) infants; it included diagnoses of fetal distress, fetal compromise, fetal bradycardia, non-re-assuring CTG.

The subgroup of 150 infants delivered for the primary indication of abnormal CTG were studied further: of these, 26 (17%) were delivered under GA and 124 (83%) under RA. There were no differences in mortality between the groups. The median (IQR) Apgar scores at 1 and 5 minutes in the GA group were 3(2-5) and 7(5-8) compared to 6(4-8) and 9(8-10) in the RA group ($p<0.001$). Oxygen administration and endotracheal intubation were also significantly more frequent in the GA group ($p=0.028$ and $p=0.002$ respectively). These findings remained significant after excluding infants who were delivered for apruptio placenta or prolapsed cord.

Conclusion:
Abnormal CTG was the predominant indication for caesarean section in preterm infants at our institution and regional anaesthesia for caesarean section is used most often. Preterm infants delivered by GA require more intensive resuscitation than those delivered by RA – a senior clinician should be present at these deliveries.

ETHICS APPROVAL NUMBER: HREC 598/2015

Title: **NUTRITIONAL INTERVENTIONS AND OUTCOMES OF CHILDREN WITH SHORT BOWEL SYNDROME AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL (RCWMCH) BETWEEN 2005 AND 2015**

Authors: Saayman, B.D.[1]; Millar, A.J.W.[2]; Van Niekerk E.[3]

Affiliation: [1]Dietetics Department. Red Cross War Memorial Children's Hospital, [2]Pediatric Surgery. Red Cross War Memorial Children's Hospital and University of Cape Town, [3]Department of Human Nutrition, Stellenbosch University

Introduction:
Short Bowel syndrome (SBS) is a malabsorption disorder which results as a consequence of extensive resection of the small bowel. This diagnosis also includes patients who are dependent on parenteral nutrition for a prolonged period due to intestinal failure. The diagnosis of short bowel syndrome is routinely made when a patient has lost > 70% of his bowel length and/or remains dependent on parenteral nutrition for longer than 6 weeks. Although the management of short bowel syndrome is multifaceted, appropriate nutritional support is considered essential as the main goal is to achieve enteral autonomy.

Objective:
The aim of this retrospective observational study was to describe the impact of nutritional interventions on the outcomes of children with SBS at RCWMCH. To evaluate the patient's parenteral Nutrition (PN) and enteral Nutrition (EN) treatment course, the factors that influence this course and complications that were associated with dietary intervention. To describe and compare the growth of children affected by SBS during their hospitalisation period and after discharge and make recommendations regarding nutritional interventions for future management.

Methods:
This was a retrospective folder review focusing on all children classified with SBS between January 2005 and December 2015. Data was collected, from their medical records, for their entire hospital stay and one month post achieving enteral autonomy.

Results:
Sixty patients were identified for inclusion but only 44 records (37 living patients, 7 deceased) were available for analysis. The average short bowel length was 61cm (range 11cm-100cm) and the main diagnosis leading to SBS in this group was necrotising enterocolitis (n=21). This was followed by jejunal atresia (n=9) and mid-gut volvulus (n=5). PN was commenced on average day 1post surgery and mean duration of PN was 104 days, with 97% of patients being able to be weaned from PN in the living group. EN was commenced on day 5 post surgery. Patients showed an average weight gain of 35g/day while admitted and 22g/day one month post achieving enteral autonomy. Length gain was shown at an average of 2.03cm per month during admission. The main complications seen were PN associated cholestasis, fat malabsorption and vitamin D deficiency.

Conclusion:
Study results shows early initiation of nutrition support and shorter dependence on PN when compared to data from similar research. Positive growth outcomes were also seen which were maintained after enteral autonomy was reached.

HREC REF: 744/2016

Title: **THE DEVELOPMENT OF AN ENGLISH HEALTH-RELATED QUALITY OF LIFE (HRQOL) MEASURE FOR VERY YOUNG CHILDREN, TO BE COMPLETED BY PROXY**

Authors: Janine Verstraete, Lebogang Ramma, Jennifer Jelsma

Background and Aims:
There is an increasing awareness that, in order to monitor health outcomes both mortality and morbidity need to be assessed. A common metric used to measure morbidity and functional limitation is the quality adjusted life year or QALY, which incorporates time spent in a health condition and Health-Related Quality of Life (HRQoL) into the measure[1]. This is of increasing importance in Low Income Countries (LIC) where programmes have been adopted and implemented to address the high burden of child mortality. The 'first 1000 days' is one such initiative which has been adopted by the WHO to improve nutritional support, health care and social support for both the mother and child. One of the aims is to improve quality of life during this vulnerable period [2]. As there is currently no appropriate measure of HRQoL in this age group, we set out to develop a valid and reliable, HRQoL instrument for children from 1 month to 3 years old, amenable to the elicitation of preference weights.

Methods:
The new HRQoL instrument, HRQoL-6D-IT, was based firstly on a systematic review of HRQoL measures for children. The next stage involved eliciting options through cognitive review from caregivers of very young children regarding HRQoL dimensions included in the EQ-5D-Y an existing validated HRQoL measure for older children. The care-givers were requested to identify items to be considered for inclusion, the wording and layout of the new measure. The item pool generated from the literature reviews and cognitive interviews were then assessed through a Delphi study with experts in the field. These items were further reduced through subsequent testing of items and retesting of a preliminary measure. The final items on the HRQoL-6D-IT included: movement, play, pain, relationships, communication and eating and, apart from pain, the descriptors referenced the behaviour of the child to age appropriate behaviour. The HRQoL-6D-IT was then tested for validity and reliability in a group of acutely-ill (AI), chronically-ill (CI) and typically developing (TD) children in two provinces in South Africa: Western and Eastern Cape.

Results:
The methodology used to identify candidate items was rigorous and yielded items which were developed to be observable with dimension descriptors referring to 'age appropriate behaviour'. Caregivers were able to reliably report on HRQoL of their very young children from age 1-36 months. The content validity had been established during the development of the instrument. Concurrent validity of the different items (dimensions) was tested between the HRQoL-6D-IT and relevant items from the ASQ, FLACC and NIPS pain scale and Diet History. The Kappa co-efficient ranged from 0.33 (fair) to 0.61 (moderate). Known groups were compared (construct validity) and the AI children had the lowest ranked VAS (median 60, range 0-100), indicating worst HRQoL and the TD group was significantly different from AI and CI ($p<0.01$) but AI and CI were not different.
The six items of the HRQoL-6D-IT were tested for internal consistency and reliability and the Cronbach's □□0.83. Test-retest results showed no variance for item scores of movement and play, and high agreement for pain (83%), relationships (87%), communication (83%) and eating (74%). The scores were highly correlated for the VAS (ICC=0.76; $p<0.001$).

Conclusion:
The HRQoL-6D-IT was found to be valid and reliable for use with children aged 1-36 months in South Africa. It is recommended the HRQoL-6D-IT be used to measure HRQoL and the impact of interventions in this vulnerable age group. It is further recommended that future testing be done to assess the feasibility and clinical utility of the measure and to include international input in further development. The lack of stability of the pain dimension needs further investigation. It is hoped that preference based weights will be developed in the future in order to facilitate cost utility analysis of interventions in this vulnerable group.

Keywords: Child, Infant, toddler, pre-schooler, Health, Health-Related Quality of Life, HRQoL, proxy

References

[1] P. J. Neumann, S. J. Goldie, and M. C. Weinstein, "Preference-Based Measures in Economic Evaluation in Health Care," *Annu. Rev. Public Heal.*, vol. 21, pp. 587–611, Jan. 2000.

[2] Human Sciences Research Council, "DST/HSCR: Human and Social Dynamics (HSD) Reseach Seminar Series: Food, nutrition and care security during the first 1,000 days," 2015.

Title: **AN ASSESSMENT OF CRITICALLY ILL CHILDREN ADMITTED TO A GENERAL HIGH CARE UNIT IN A REGIONAL HOSPITAL IN THE WESTERN CAPE, SOUTH AFRICA**

Authors: Drs R Vosloo (Registrar), S Salie (Consultant, supervisor), WJ Breytenbach (Consultant, on-site supervisor)

Objective:
To determine the outcomes of children admitted to a general high care unit (adult and children) in a regional hospital in the Western Cape, South Africa. The Paediatric Index of Mortality 3 (PIM3) mortality prediction score and Standardized Mortality Ratio (SMR) will also be calculated.

Methods:
The study was an observational analysis of all critically ill children (<13 years of age) admitted to the High Care Unit (HCU) of George Regional Hospital in the Western Cape during a one-year period (2016). Patient age, gender, HIV and nutritional status, immunization status, diagnoses, interventions in the form of inotropes and respiratory support, hospital and critical care unit length of stay and admission times, referral data to the tertiary paediatric intensive care unit (PICU), as well as outcomes (death/survival) in all children including those suffering from surgical problems, were analysed. The PIM3 score was calculated in all admissions and compared to the actual mortality rate to determine the Standardized Mortality Ratio (SMR).

Results:
There were 144 admissions of which 2 were readmissions within 48 hours of discharge from the HCU. The median age was 9 months (interquartile range [IQR] 2 to 40 months). An equal male to female ratio was observed. Twenty-nine (20%) of the patient cases were transferred to the tertiary PICU. Twelve (8%) patients died, of which 3 died at the tertiary hospital (Red Cross War Memorial Children's Hospital). Of the 12 deaths, 6 (50%) died of sepsis, 3 (25%) of respiratory failure and 3 (25%) of diarrheal disease. No Surgical or trauma related deaths were observed.

The median length of admission to George Regional Hospital was 6 days (IQR 2 to 12 days). Seventy percent of the admissions to the HCU occurred after-hours. The median length of stay in the HCU was 1 day 17 hours (IQR 1 to 3 days). The median time awaiting transfer to the tertiary PICU was 12 hours (IQR 7 hours to 1 day). There was a more than 48-hour delay in transfer of 12 of the patient cases. Of the 12 cases, 5 (42%) were delayed due to tertiary bed availability, 5 (42%) being too unstable for transfer, 1 due to unsuitable weather conditions and 1 with no specific reason noted for delay. Of the 29 patients referred to the tertiary PICU, the median length of tertiary unit stay was 6 days (IQR 3 to 12 days). Data of tertiary length-of-stay was not available for 7 patient cases.

Ninety-three (65%) of the 144 HCU admission cases required respiratory support in the form of continuous positive airway pressure (CPAP) and/or invasive ventilation. The median length of time requiring respiratory support was 4 days (IQR 1 to 7 days). Data was not available for 3 of the 93 cases. Sixty-five (45%) of the patient cases required inotropic support. The median time requiring inotropic support was 2 days (IQR 1 to 4 days).

The cumulative PIM3 probability of death score was 9.049. An SMR of 1.326 was thus observed.

Conclusion:
Critically ill children admitted to George Regional Hospital are likely to require specialised care in the form of either ventilation and/or inotropic support. A good channel of communication and transport to the tertiary PICU is necessary to provide optimal care to these children at regional level. Most of the children (92%) admitted to the HCU were successfully discharged.

Title: **AUTOIMMUNE HEPATITIS IN CHILDREN: EXPERIENCE IN RED CROSSS WAR MEMORIAL CHILDREN'S HOSPITAL CAPE TOWN**

Authors: Yassin SAA,[1]De Lacey RJ,[1] Pillay K,[2] Goddard EA[1]

Affiliation: [1]Division of Paediatric Gastroenterology, Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital/University of Cape Tow
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Introduction:
Autoimmune hepatitis (AIH) is a chronic progressive immune mediated liver disease, characterized by favorable response to treatment.
There is paucity of data about its profile in sub-Saharan Africa. The current study aimed to describe the socio-demographic as well as clinical characteristics, diagnostic criteria, treatments and possible outcomes of children diagnosed with AIH at Red Cross War Memorial Children's Hospital (RXWMCH).

Methods:
A cross sectional descriptive study of children diagnosed with AIH attending RXWMCH from 2005 to 2015 was carried out. Ethical approval for the study was obtained from the University of Cape Town/RXWMCH.
Relevant patient's data was retrieved from the hospital's medical records as well as GIT Unit's and histopathological databases.
Data was analyzed using SPSS version 24.0 ($p<0.05$).

Results:
A total of thirty-nine patients were studied. Majority were female 28(76.9%), mean age at presentation was 7.27 years. Jaundice 32(89.7%) and hepatomegaly 32(84.6%) were the most common presenting symptom and sign respectively. Majority 26(66.7%) presented in acute hepatitis.
17(47%) had AIH1 while one patient (2.5%) had AIH2, however half of the subjects (50%) were auto-antibodies negative. Out of the 25 who had MRCP done seventeen (43.6%) had associated sclerosing cholangitis
37(94.9%) responded to steroid therapy with 31(80%) having normalized transaminases
Predictors of good response to treatment were high transaminases, early stage of cirrhosis, platelet count, age at diagnosis, albumin & Gama globulin level. At 4.38 years' mean follow up 20(51.3%) maintained their remission, 10(25.6%) relapsed, 7(17.9%) failed to normalize their transaminases out of which 6 (16.6) were started on second line medications (MMF, tacrolimus), one (2.6%) received liver transplantation while one (2.6%) died.

Conclusion:
Paediatric AIH responds well to immunosuppressive therapy with good survival.
Hence AIH should be considered in the work up of any child with hepatitis irrespective of mode of presentation in order to apply therapy timeously to save lives.

Title: **WHAT DOES CARE THROUGH FAMILY IN AFRICAN HEALTH CARE SETTINGS LOOK LIKE? PRELIMINARY FINDINGS FROM A QUALITATIVE OBSERVATIONAL STUDY**

Authors: Candice Bonaconsa, Angela Leonard, Natasha North, Stephanie Sieberhagen and Minette Coetzee

Objective:
The application of quality improvement tools developed in higher-income countries within African settings can be problematic because of differences in need, resourcing, staffing, and professional, organisational and social cultures. In the African context which is characterised by high burden of childhood diseases and high child population rates, nurses comprise the majority of the healthcare workforce. There is a need for contextually and culturally specific evidence relating to effective and safe ('best') practice in nursing hospitalised children. The Child Nurse Practice Development Initiative designed a multi-site research study to observe children's nursing practice and how parents are involved in the care of their children. The study aimed to explore and describe the clinical practice models of health care providers who work with families to care for children in four healthcare settings.

Methods:
An appreciative inquiry approach was used. Data were collected using participatory qualitative methods of case study interviews, focus groups, sociograms, photographic interviews and participant observations at four research settings. Using an iterative approach, comment was continuously invited from participants. Using the pathway of care and graphic facilitation enhanced group participation and strengthened the voice of appreciative inquiry.

Results:
Data suggested that there were elements and characteristics evident in the practice of children's nurses which were quite distinctive when compared to practices in higher resourced health care settings. This was especially evident in the way that nurses collaborated with mothers to care for hospitalised children, and accepted the mothers' presence as a cultural norm and a logical necessity. Data analysis yielded six initial themes, providing the basis for further development of a local model of best nursing practice.

Conclusions:
The intentionally participatory and visual research methods have generated a rich data set from mothers, nurses and doctors as they recognised, described and reflected on aspects of their practice. Initial outcomes have helped to make implicit practices explicit and contribute to the generation of contextualised and culturally appropriate evidence. Outcomes also provide the basis for the design of a self-administered questionnaire that could support future quality improvement interventions in local settings.

HREC approval number: 752/2015

Title: **THE USE OF INHALED NITRIC OXIDE TO TREAT PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN IN A TERTIARY PUBLIC HOSPITAL IN SOUTH AFRICA FROM 2010-2014: MORBIDITY, MORTALITY AND COST**

Authors: McAlpine A., Horn A., Tooke L.

Background:
There is insufficient evidence that inhaled nitric oxide (iNO) reduces the mortality of persistent pulmonary hypertension of the newborn (PPHN) when extracorporeal membrane oxygenation (ECMO) is not available. Some hospitals in South Africa have access to iNO for PPHN, but not ECMO. Sildenafil is an alternative to iNO, but there are insufficient data to inform management of neonates treated with iNO, with or without sildenafil, in this setting.

Objectives:
(i) To describe the characteristics at birth, clinical course, and short-term outcomes of a cohort of term and near term neonates with PPHN, who were treated with iNO, with or without sildenafil, in a tertiary neonatal unit; (ii) to determine if any variables were associated with mortality; (iii) to describe the relationship between the use of sildenafil and cost of care, represented by the duration of intubation and iNO use; and (iv) to describe the frequency of sildenafil prescription.

Methods:
A retrospective review was carried out on folders of neonates with PPHN who were treated with iNO in Groote Schuur Hospital, Cape Town, South Africa, between January 2010 and December 2014.

Results:
Forty neonates were included; 85% were full term. Meconium Aspiration Syndrome (MAS) was the commonest cause of PPHN (50%), followed by intrapartum hypoxia (20%), sepsis (17.5%), pulmonary hypoplasia (7.5%) and idiopathic (5%). Fourteen neonates (35%) died. Pulmonary hypoplasia and pneumothorax were associated with mortality ($p=0.037$ and $p=0.004$ respectively). An FiO_2 of 1.0 and an iNO dose of $\geq$ 20 ppm at 24 and 48 hours respectively, predicted death (specificity 89% vs. 100%, sensitivity 67% vs. 43% and $p=0.003$ vs. $p=0.007$ respectively). Sildenafil was prescribed more often after 2011 (83% vs. 65%) and was associated with increased survival ($p=0.018$) – early administration was associated with a shorter time to extubation ($p=0.012$) and a shorter course of iNO ($p=0.044$).

Conclusion:
The treatment of PPHN with iNO in the absence of ECMO was associated with high mortality, particularly neonates with congenital lung abnormalities. The FiO_2 and iNO requirements at 24 and 48 hours respectively could be used to identify neonates who are unlikely to benefit from continued treatment. Sildenafil was prescribed with increasing frequency during the study. The combination of iNO with sildenafil was associated with more cost-effective care and improved short term outcomes. These findings provide a potential basis for cost-saving measures and resource allocation

Title: **MORBIDITY AND MORTALITY FROM ROAD TRAFFIC CRASHES IN CHILDREN IN METRO WEST, CITY OF CAPE TOWN – 2014**

Authors: Zulfah Albertyn-Blanchard, Shanaaz Mathews, David Coetzee, Sebastian Van As

Objectives:
To assess the fatal and non-fatal pattern of road traffic crash (RTC) injury burden of children under 13 years old from Metro West, City of Cape Town.

Methods:
A sub-set for RTC data was extracted from the 2014 Child Death Review (CDR) study and 2014 Childsafe South Africa (CSA) dataset. All fatal and non-fatal RTC injuries were stratified by age, sex and mechanism of RTC within the Metro West, City of Cape Town, from 1 January until 31 December 2014. RTC mortality rate was estimated in addition to premature mortality by means of years of life lost. RTC morbidity was determined by means of years of life lived with disability relative to the nature of injury and hospital admission.

Results:
There were 37 fatal cases from the CDR dataset and 695 non-fatal cases from the CSA dataset. The overall RTC mortality rate was 8.7 per 100 000 population and pedestrian fatalities accounted for the greatest proportion of premature mortality (84.2%). The greatest proportion of fatal and non-fatal RTC injuries was observed in children aged 5-9 years. The leading form of injury across all ages for both fatal and non-fatal RTC injuries was a head injury. Majority of children involved in a non-fatal RTC injury suffered from moderate injuries (49%). Fractures contributed to the highest years of life lived with disability rate, peaking in children aged 5-9 years (4.4 YLD per 100 000).

Conclusions:
Our study has found that for both fatal and non-fatal RTC injuries, majority of children were male pedestrians aged 5-9 years old. To attenuate the RTC burden for children, preventative initiatives need to be evidence based and targeted at geographic areas where this burden is the greatest.

Title: **THE PREVALENCE OF FOOD ALLERGY AND FOOD SENSITISATION IN URBAN AND RURAL SOUTH AFRICAN TODDLERS**

Authors: Botha M, Basera W, Facey-Thomas, Gray CL, Kiragu W, Lunjani N, Ramjith J, Watkins A, Levin ME

Background:
This study aimed to determine and compare the prevalence of food sensitisation and challenge proven IgE mediated food allergy in urban and rural South African toddlers aged 12-36 months.

Methods:
In this cross-sectional study of unselected children, 1185 participants were included in urban Cape Town and 398 in the rural Eastern Cape district of Mqanduli. The urban cohort of 1185 participants was representative of the Cape Town population according to the most recent census. The rural cohort comprised 398 Black African (BA) participants. All participants' parents completed a questionnaire and the children underwent skin prick tests to egg, peanut, cow's milk, fish, soya, wheat, and hazelnut. Participants with SPT≥ 1mm to one or more foods and not clearly tolerant on history underwent an open oral food challenge (OFC).

Result:
The prevalence of challenge proven food allergy was 2.3% (CI 1.5-3.7) in urban children. The most common allergy was to egg (1.8%), then peanut (0.7%) followed by cow's milk (0.1%) and fish (0.1%). Urban sensitisation (≥1mm SPT) to any food was 11.4% (CI 9.6-13.3) and at ≥3mm SPT 9.0% (CI 7.5-10.8). There were no statistically significant differences in food allergy prevalence between children of different ethnic groups in Cape Town. The rate of sensitisation at ≥1mm SPT and ≥3mm SPT to any food, peanut and egg was higher in urban Black African participants than Caucasian participants and participants of mixed ethnicity. This difference was only statistically significant for ≥1mm SPT sensitisation to egg. In the rural BA cohort 0.5% (CI 0.06-1.8) of children were food allergic - all to egg. This is significantly lower than the prevalence in the urban cohort overall (2.3%) and in urban black African participants (2.7%; CI 1.5-4.5).

Conclusion:
Food allergy prevalence and levels of sensitisation amongst urban children in Cape Town are comparable to the prevalence in other industrialised middle income countries and are significantly higher than in rural areas. Further analysis will describe and compare environmental exposures and other risk factors in this cohort.

HREC 038/2012

Title: **DELINEATION OF THE GENETIC CAUSES OF EPILEPTIC ENCEPHALOPATHY IN SOUTH AFRICAN PAEDIATRIC PATIENTS**

Presenter: Alina Esterhuizen

Objective:
Sub-Saharan Africa bears the highest burden of epilepsy in the world as a consequence of high incidence of CNS infections, perinatal insults and traumatic brain injury. Genetic epilepsy is underdiagnosed due to lack of awareness and unavailability of genetic testing for epilepsy. In this study we aim to describe the genetic architecture of severe infantile seizure disorders in South African patients and establish a framework for genetic testing in South Africa and Africa more broadly.

Methods:
We recruited 92 South African children diagnosed with epileptic encephalopathy (EE), on the basis of clinical semiology and neurophysiological studies: 46 Indigenous Black, 35 Mixed Ancestry and 11 Caucasian South African children. Of these, 21 were clinically suspected to have Dravet Syndrome (DS). Targeted resequencing of 71 known EE genes and chromosomal microarrays were deemed appropriate, was performed. Patient recruitment is ongoing and we aim to recruit and test 200 patients (HREC REF 232/2015).

Results:
Pathogenic *de novo* mutations were identified in 26 patients. *SCN1A* mutations were found in 9/22 (41%) of the Dravet group, which was markedly less than the published frequency of *SCN1A* mutations in DS. Clinical reassessment with the screening test by Hattori et al., (2008) resulted in a changed working diagnosis of 5 *SCN1A*-negative patients in the Dravet group. *SCN1A* variants were also found in 2 patients of the remaining cohort, who are undergoing clinical reassessment emphasising the value of a genetic diagnosis. In the larger cohort, likely pathogenic changes were detected in 16 patients. A 16p13.11 deletion was detected in 1 patient, additional microarray analysis is ongoing.

Conclusion:
These results carry implication for patient management and present valuable insights into disease presentation, motivating translation into diagnostic practice even in the resource-limited African setting. This is the first genetic research study of epilepsy in South African patients.

Title: **SUDDEN UNEXPECTED DEATHS OF INFANTS: THE VALUE OF A MOLECULAR AUTOPSY**

Authors: Laura Heathfield, Raj Ramesar and Lorna Martin

Affiliation: Division of Forensic Medicine and Toxicology, Department of Pathology, Faculty of Health Sciences, University of Cape Town, Anzio Road, Observatory, 7925; South Africa

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Objective:
At Salt River Mortuary, more than 250 sudden unexpected infant death cases are investigated annually. Following autopsy most of these cases are classified as natural, with infectious causes of death. However, the presence of predisposing genetic factors towards infant death is an emerging field and has not yet been investigated in a local context. The aim of this study was to demonstrate the value of a molecular autopsy to establish the underlying genetic contributions towards sudden unexpected death of infants.

Methods:
A complex research framework, aligned with service operations and ethical standards, was first established as Salt River Mortuary. Using this framework, a cohort of infants was established (n=108); all who died suddenly and unexpectedly and who were examined at Salt River Mortuary between 1 March 2016 – 30 June 2017. Parents of infants gave informed consent to participate. During post-mortem investigation, a blood sample was obtained for research purposes. DNA was isolated from blood samples and a fragment within the *toll-like receptor-4* (*TLR4*) gene was amplified and a genetic variant (NM_138554.3: c.896A>G rs4986790) within the fragment was genotyped.

Results:
Seven of the 108 infants were heterozygous for the genetic variation (NM_138554.3: c.896A>G rs4986790) in *TLR4*. TLR4 is a receptor that activates an immune cascade in response to bacteria and some viruses, and the variant observed in this study is predicted to have a pathogenic clinical significance. Due to the complexities of the immune system, this genetic variant is unlikely to have been solely responsible to cause death; rather the presence of the genetic variant may have contributed towards a predisposition in the immune response of the infants – which may give additional weight to a respiratory-related cause of death.

Conclusions:
These findings demonstrate a proof of concept for molecular analysis to be included in post-mortem investigations, especially in sudden unexpected death of infant cases. Due to the heritability of genetic variants, such results would be of significant value to living relatives and to parents who plan on having additional children in the future.

Ethics: This study has obtained ethics approval from the University of Cape Town Faculty of Health Science Human Research Ethics Committee (HREC REF: 445/2015).

Acknowledgements: Lerato Maraja, Kate Reid, Caitlin Herbert

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Project presentation history: A component of this new research has been presented at the African Society of Forensic Medicine conference in March 2017

Title: **A REVIEW OF THE USE OF HIGH FLOW NASAL CANNULA OXYGEN THERAPY IN HOSPITALIZED CHILDREN AT A REGIONAL HOSPITAL IN THE CAPE TOWN METRO, SOUTH AFRICA**

Authors: Elizabeth Hoffman, MBChB (US) DCH; Kirsten L. Reichmuth, MBChB (UCT) MPH (UCT) Melissa L. Cooke, MBChB (UCT) FCPaed (SA)

Background:
High-flow nasal cannula oxygen (HFNC) is a non-invasive alternative to nasal continuous positive pressure oxygen (CPAP) therapy for infants and children requiring respiratory support. There is a paucity of literature to support its use in children, with no published data from sub-Saharan Africa.

Objective:
To describe the outcomes and adverse events of HFNC in the first year of its use in a level two (L2) general paediatric ward, compared with outcomes of an historical cohort when this intervention was unavailable.

Methods:
This retrospective descriptive study included children aged <13 years who received HFNC in the first 12 months after its introduction (HFNC-availability group; *n*=66). Demographic data, clinical characteristics, and outcomes (death, treatment failure, length of HFNC, and HFNC-related adverse events) were assessed. A comparative description of children that required transfer to level 3 (L3) for respiratory support (more than available standard low-flow oxygen) in the 12-month period prior to HFNC availability (pre-HFNC group; *n*=54) was performed and outcomes were compared using standard descriptive and comparative statistics.

Results:
The median age of the cohort was 5 months (interquartile range [IQR] 1.9–14.6). Sixteen children (13.3%) were malnourished, 10 (8%) were HIV infected, and 30 (25%) were ex-premature infants. The most common diagnoses were pneumonia, bronchiolitis, and asthma. Asthma, anaemia, and cardiac abnormalities were the most prevalent underlying co-morbidities. Two children died in each group.
All 54 children in the pre-HFNC group were transferred to L3; 38 (70.4%) needed CPAP or invasive ventilation. In the HFNC-availability period, 85 children were assessed as needing more than standard low-flow oxygen therapy: 19 were immediately transferred to L3 where 17 (89.4%) received CPAP or invasive ventilation; 66 received HFNC at L2, 16 (24.2%) of these children required transfer to L3 for CPAP or invasive ventilation.
The median duration of HFNC was 46.3 h (IQR 19.5–93.5) overall, and was 12 h (IQR 39.5–106) and 58.5 h (IQR 39.5–106) for those who failed or were successfully managed on HFNC, respectively. No HFNC-related serious adverse events were recorded at L2.

Conclusion:
HFNC is a safe, effective, feasible option for non-invasive ventilation of children with respiratory illnesses in a resource-limited L2 setting. A greater proportion of children admitted with lower respiratory tract infections required support in the HFNC-availability group, but the intervention reduced the bed-pressure on L3. Improved identification of HFNC failures and better adherence to the protocol is needed at L2.

Title: **PERSISTENT INCREASE OF MATRIX METALLOPROTEINASES IN THE CEREBROSPINAL FLUID OF PAEDIATRIC TUBERCULOUS MENINGITIS**

Authors: Joshua Li, Ursula Rohlwink, Anthony Figaji

Objective:
Tuberculous meningitis (TBM) commonly affects children in TB endemic areas, and is associated with a high morbidity and mortality. Matrix metalloproteinase (MMPs) concentrations are elevated in the cerebrospinal fluid (CSF) of adult TBM patients, and associated with neurological complications. However, to date, these have not been studied in paediatric TBM. This study aimed to quantify and measure the temporal profile of specific MMPs and their inhibitors in paediatric patients with TBM, and to draw associations to the clinical parameters.

Methods:
In this study, lumbar and ventricular cerebrospinal fluid (CSF) as well as serum were collected in 40 children treated for TBM at the Red Cross War Memorial Children's Hospital (RCCH). MMP-9, MMP-2, and their tissue inhibitors, TIMP-1 and TIMP-2, were quantified using Luminex® technology and compared to controls. Clinical data, including admission characteristics, radiological and chemistry data, were also collected.

Results:
We found that the lumbar MMPs and their inhibitors were significantly increased relative to controls, while the ventricular and serum samples showed mixed results. A decrease in lumbar MMP-9 was seen after commencement of TB treatment. The lumbar compartment proved the most promising for analysis purposes. Association analyses found positive correlations between MMP-2 and TIMP-2, and negative correlations between MMP-9 and TIMP-1. Contrary to previous studies in adults, an overall increase in MMP-9 levels during hospital stay was associated with a good outcome at 6 months (RR: 2.1; CI: 1.231 – 3.528; *p=0.008*). No significant association with outcome was found with the other analytes.

Conclusions:
This study found that: 1). MMPs and their inhibitors were persistently elevated in paediatric TBM, with a 2) significant drop in MMP-9 levels early in treatment. The analytes were 3) not found to be associated with neurological complications or poor outcome and contrarily, 4) an increase in MMP-9 during hospital stay was associated with better outcomes. Finally, 5) our data could offer new insight into the roles of MMPs and TIMPs in the pathophysiology of, and possibly recovery from, paediatric TBM.

Title: **ALPHA GAL ALLERGY IN RURAL BLACK AFRICAN SUBJECTS ASSOCIATED WITH A HIGH PREVALENCE OF ABDOMINAL MANIFESTATIONS AND A MORE RAPID ONSET OF SYMPTOMS**

Authors: [1]T. Mabelane, [1]M. Botha,[1] H. Facey Thomas, [1]M. Levin.

Affiliation: [1]Department of Paediatric Allergology, Red Cross Children's Hospital, University of Cape Town, South Africa.

Rationale:
There is an association between adverse reactions to red meat and mammalian oligosaccharide epitope, galactose-alpha-1, 3-galactose (alpha-gal) allergy. Reports were received of high prevalence of meat allergy in black African subjects in the rural Eastern Cape Province of South Africa.

Methods:
This was a cross-sectional study conducted in the 1 month period of July 2017, in the Mqanduli district of the rural Eastern Cape. Questionnaires assessed symptoms to meat ingestion. Sensitisation was confirmed with ImmunoCAP® to alpha-gal. Oral Food Challenge (OFC) to beef sausage (dose calculated according to weight) was used as the golden tool to diagnose alpha-gal allergy.

Results:
67% were female; median age was 12 years (IQR 8-25). 90.6% reported multiple reactions and 7.1% a dose response. Median delay from 1st symptoms to diagnosis was 6 years(IQR 3-8). The most recent reaction prior to diagnosis was experienced at a median of 1 year (IQR 0-5). 10.6% recalled tick bites (no people noted reactivation of tick bite site on meat ingestion), 48.2% scabies, 24.7% worms and 9.4% bilharzia. Alpha-gal IgE ranged between 0.7 and 663 kU/L (median 11.9, IQR 4.1-32.8). Alpha-gal: total IgE ratio ranged from 0.1 to 67.9% (median 4.3; IQR 1.8-11.0). 83 participants were diagnosed with alpha-gal allergy by OFC using predetermined major and minor objective criteria resulted inabdominal symptoms (abdominal pain, vomiting, diarrhoea) in 77.1%, skin reactions (scratching, hives, erythema or angioedema)in 51.8% and severe reactions (respiratory symptoms or hypoperfusion) in 6%, from 45 to 375 minutes (median 105; IQR 85-135) after ingestion. 2 participants were diagnosed with alpha-gal allergy by very high alpha-gal IgE and alpha-gal: total-IgE ratio with recent severe symptoms.

Conclusion: Alpha-gal allergy in 85 rural black African subjects showed rapid onset of symptoms and a high prevalence of gastrointestinal manifestations.

Title: **MANAGING TAKAYASU ARTERITIS IN THE CARDIAC CATHETHERISATION LAB – THE CAPE TOWN EXPERIENCE**

Authors: Swanson L [1,2] , Fourie B [3] , Nourse P [4] , McCulloch M [4] , De Decker R [2]

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[4] Red Cross War Memorial Children's Hospital, Dept of Paediatric Nephrology, Rondebosch Cape Town, South Africa

Background:
Takayasu arteritis is a chronic inflammatory disease of the aorta and pulmonary arteries and their major branches. The disease typically affects young adult females, but may also manifest in childhood. Vascular complications are common, and range from aneurysmal dilation to severe stenosis with visceral ischaemia. Management of this large vessel vasculitis has relied on immunosuppressive therapy and adjunctive surgical revascularisation strategies to control and improve renovascular complications. Alternative approaches such as catheter-based interventions have been shown to be effective in managing its vascular complications in adult patients. Little data exist for this strategy in the paediatric population.

Objective:
To describe the management and outcomes of a cohort of young patients with Takayasu's arteritis using endovascular techniques commonly employed for interventional cardiac catheterization procedures.

Methods:
Eleven patients with significant stenosis on CTA / MRA underwent catherization for revascularization procedures. Patients either received percutaneous transluminal angioplasty of the affected vessel or had an arterial stent placed. The preferred management approach was decided upon at the discretion of the attending cardiologist. Patients with significant stenoses at follow up were considered for additional procedures.

Results:
A total of 9 procedures were performed. Four patients were successfully stented using either Advanta V12 (covered) or Cook Formula stents. Of these, one patient suffered undetected retroperitoneal bleeding, and demised several hours after stenting of the descending aorta. Two patients required subsequent stenting procedures to alleviate stenoses that developed after their initial procedures, with good results. Three patients underwent renal artery angioplasty, with no reported complications. Follow up revealed significant improvements in symptoms, blood pressure control, and renal function.

Conclusion:
Transcutaneous arterial intervention is an effective non-surgical strategy for relieving the vascular complications of Takayasu's arteritis in children.

Title: **PAEDIATRIC RHEUMATOLOGY ACCESS IN THE DEVELOPING WORLD: REFERRAL PATTERNS TO A TERTIARY PAEDIATRIC RHEUMATOLOGY SERVICE IN CAPE TOWN**

Authors: Waheba Slamang and Chris Scott

Affiliation: Department of Paediatric Rheumatology, Red Cross War Memorial Children's Hospital, University of Cape Town

Background
Paediatric rheumatology (PR) is not a health care priority in South Africa. Here resources are primarily (and appropriately) channelled towards reducing the high burden of infectious diseases.
In view of current and expected future resource limitations, referral patterns need to be better understood to achieve early detection and referral of PR patients for optimal management and improved outcomes. Opportunities to expand the network of health care professionals involved in PR care should also be identified to achieve this.

Objective
To describe the geographic household location of patients referred to the PR service in Cape Town and elucidate the sources of referral

Methods
A systematic retrospective case file review of all patients attending the Cape Town paediatric rheumatology service for treatment and diagnosis between 2010 and 2015 was conducted.
Household locations were plotted onto an area map of South Africa and those in the Western Cape, divided according to municipality. Households situated in the City of Cape Town municipality, were further divided according to health sub-district.
The sources of referral were documented in terms of referral institution, public or private health care and health worker qualification.

Results
533 patients were included in the study - 213 (40%) males and 320 (60%) females. The median age and duration of symptoms at first consultation in the Cape Town PR service was 108 months (IQR 57 – 138 months) and 6 months (IQR 2- 12 months) respectively. An increasing number of patients, 406 (76.2%) with rheumatic and 101 (19%) non-rheumatic conditions were referred. The diagnosis was uncertain for 26 (4.8%) patients. 502 (94.2%) patients were resident in the Western Cape of which 458 (91.2%) were located in the City of Cape Town municipality. The combined Southern and Western health sub-districts of the City of Cape Town municipality, referred a significantly higher percentage of patients under 16 years, compared to the other municipalities in the Western Cape ($p= 0.0025$). 21 patients (0.04%) were referred from the Eastern Cape, 8 (0.02%) from Gauteng and 2 (0.004%) from Kwazulu-Natal.
Referral data was documented for 445 of 533 referrals. 279 (62.7%) referrals were from the public health sector, of which 187 (67%) were from paediatric services.
166 (37.3%) referrals were from the private health sector, 65 (39.2%) from paediatricians. There were no referrals from nurses at the community health centres.

Conclusion
The recent establishment of a paediatric rheumatologist led tertiary clinical service in Cape Town, has increased the awareness of PR diseases and the subsequent referral of patients in the surrounding health districts.
These findings support further input into the development of PR referral systems, including the education of health and allied health care professionals at all levels of care.

Title: **CHARACTERISTICS OF CHILDREN PRESENTING WITH CARDIOMYOPATHY IN AN AFRICAN SETTING – INITIAL FINDINGS OF THE IMHOTEP REGISTRY**

Authors: George Comitis[1], Barend Fourie[2], Sarah Kraus[3], Alexia Joachim[1], Liesl Zuhlke[1,3], John Lawrenson[1,2]

Affiliation: [1]Red Cross War Memorial Children's Hospital, Cape Town, South Africa and University of Cape Town
[2]Tygerberg Hospital, Cape Town, South Africa and University of Stellenbosch
[3]Groote Schuur Hospital, Cape Town, South Africa and University of Cape Town

Background:
Cardiomyopathy remains a leading cause of morbidity and mortality in children worldwide. Although we see 30 – 40 incident cases annually in Cape Town, the characteristics of childhood cardiomyopathies in African children have not been systematically described. IMHOTEP is the first prospective, open-ended registry of prevalent and incident cases of heart muscle disease in children and adults in Africa. It will expand from pilot sites in Cape Town to other centres in South Africa and subsequently the whole continent to accurately characterize cardiomyopathies in Africa. This report describes the experience to date from the first paediatric sites.

Methods:
Commencing September 2016, all incident cases of cardiomyopathy or myocarditis presenting to two referral paediatric cardiac centres were enrolled into a dedicated OpenClinica registry (IMHOTEP African Cardiomyopathy and Myocarditis Registry). Details captured include demographics, history, physical examination, blood investigations, genetic screening, chest X-ray, ECG, echocardiogram features and outcome measures (adverse events, hospitalizations and death). Children were enrolled at Red Cross Children's and Tygerberg Hospitals.

Human Research Ethics Committee approvals were obtained prior to implementation of the registry.

Results:
As of July 2017, twenty-five patients have been enrolled prospectively into the registry. Baseline demographic characteristics, modes of initial presentation and adverse outcomes were recorded. In total, 11/25 (44%) of the patients are infants. Four of the 25 patients (16%) are perinatally HIV exposed, but all four tested negative by PCR. The predominant cardiomyopathy phenotype is dilated cardiomyopathy – 12/25 (48%) followed by myocarditis (biopsy-proven, suspected clinically or on CMR) – 7/25 (28%). Morbidity and mortality to date has been substantial – seven deaths (mortality 28%), average hospitalizations 2.7/patient, average ICU admissions 1.3/patient, and mean number of days in hospital 28.6 (SD 17).

Conclusions:
Already in these early stages of the registry, we are seeing the full range of cardiomyopathy phenotypes represented in African children and a significant mortality and morbidity. The paediatric limb of the IMHOTEP African Cardiomyopathy Registry promises to be a powerful tool to characterize childhood cardiomyopathy in Africa with the ultimate aim of improving prevention and management of this often devastating childhood illness.

Title: **A RETROSPECTIVE STUDY TO ASSESS THE VALUE OF MASS SPECTROMETRY IN THE MANAGEMENT OF PAEDIATRIC POISONING AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL**

Authors: Norbertta Washaya[1,2], Alicia Evans[3,4], Rudzani Muloiwa[2,4], Peter Smith[3,4] and Heloise Buys[1,2]

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Introduction:
Unintentional paediatric poisoning is not an uncommon emergency centre presentation. In 2004, it was responsible for 10.9% of all global unintentional injuries in children less than 15 years. The role of investigations, specifically the use of Mass Spectrometry, in paediatric poisoning remains controversial. There is a paucity of data on the role of investigations in the management of paediatric poisoning in low and middle income countries.

Objective:
The objective of the study was to assess the value of mass spectrometry in the management of paediatric poisoning at RCWMCH.

Methods:
A retrospective cross-sectional analysis of patient folders was carried out between 22 November 2015 and 31 December 2016. All patients with suspected unintentional or intentional poisoning who presented to Red Cross War Memorial Children's Hospital(RCWMCH) during the one-year period and had a urine sample sent for toxicology using the Mass Spectrometer at the Division of Clinical Pharmacology Groote Schuur Hospital, were recruited. Data collected included patient demographic data, clinical features, investigations, management and outcome and were described using conventional statistical methods. All toxins detected by routine toxicology and/or mass spectrometry were described. Proportions and their 95% confidence intervals in outcomes of interest were used to depict frequencies of categorical variables, while medians with interquartile ranges were used to summarise all continuous variables.

Results:
Of the 67 patients that were recruited 36 (54%) were female. Their median age was 59.5 (IQR 22.6 -108.2) months. The primary care giver was the mother in 74% (49/66) of the patients. In 44(69%) children, clinical suspicion after examination led to a sample being sent for mass spectrometry toxicology screening whilst witnessed toxin was found in 4 patients. Patients self-referred in 36% (24/67) of cases. The most common presenting complaint was neurological in 89% (64/67), with 38% (24/64) children having an altered level of consciousness. Point-of-care toxicology was positive in 9/36 (25%) cases tested. Mass Spectrometry could identify the presence of an unintentionally ingested drug in 66% (43/64) of the samples tested. Definite toxin ingestion was found in 29/64 (45%) children, and not likely in 35/64 (55%) cases. Medical management was mainly supportive, with specific antidotes given in 10/62 (16%) of cases. Life support was instituted in three children as a result of toxin ingestion, however individualized social interventions were instituted in most patients after a positive result. The four deaths recorded in this study population, were not due to poisoning.

Conclusion:
Suspected paediatric poisoning is common and the symptoms are not specific and may frequently include neurological symptoms. Mass Spectrometry is useful as a confirmatory test in children who present with suspected drug poisoning and becomes invaluable when its use is targeted to child protection. Prospective studies would be useful to evaluate its use further in children.

Ethical Approval number 742/2016

Title: **USE OF 'HOME-MADE PD' ADAPTED INTRAVENOUS FLUID SOLUTION FOR ACUTE PERITONEAL DIALYSIS IN AFRICA**

Authors: McCulloch MI, Nourse PJ, Argent AC.

Objective:
Peritoneal Dialysis (PD) is used for the treatment of Paediatric Acute Kidney Injury (AKI) but is usually dependant on commercially manufactured peritoneal dialysis fluid and surgically inserted PD catheters. In less well-resourced countries in Africa there is limited availability of commercially produced PD fluid (currently only 1 manufacturing plant in the whole of Africa based in SA (Adcock Ingram) with the rest of the countries having to import fluid from overseas. In addition, there is also a shortage of trained surgeons to place such PD catheters which results in the limitation of the use of this modality where no PD or Haemodialysis is available.

Methods:
Retrospective audit of paediatric AKI cases in which acute PD was used at Red Cross Children's Hospital from 1999 – 2014 for cases with severe acidosis:

1. Using adapted intravenous fluid solution by adding 50% Dextrose to a Balanced Electrolyte Solution(Balsol) for use as PD solution
2. Bedside PD catheter insertion by paediatricians/intensive care physicians

Results:
A total number of 611 cases reviewed who underwent acute peritoneal dialysis during 1999 – 2014. Sub-group of 49/336(14.6%) cases between 2002 – 2009 received Home-made PD fluid for severe acidosis.

- Causes of AKI included cardiac, gastroenteritis, sepsis, metabolic, pneumonia, HUS and other.
- Indications: Intractable acidosis unresponsive to medical therapy(Bicarbonate and diuretics) together with conventional indications of dialysis in AKI (anuria/oliguria and/or hyperkalaemia)
- Gender M:F 21:28
- Age: Range Newborn – 10.2yrs, Mean 1.13years (Alive 1.26yrs. Died 1.09yrs)
    - Median 0.33year (3 months).
    - Neonates 17 cases. Infants (<1 year) 40 cases. Cardiac cases 9
- Weight: Range 1.3 – 50kg, Mean 13.4kg, Median 4.1kg
    - <2kg 5 cases, 2-<5kg 19 cases, 5-<10kg 17 cases, 10-<20kg 4 cases, >20kg 3 cases
- Fluid Complications: Infection – 2/28(7%) only with only 1 case related to dialysis
    - Electrolyte abnormalities – nil
- Length of PD: 1 to 17 days. Mean 3.9days. Median 3 days
- Type of PD: Manual PD 37/49. Automated 12/49(Paxtra 1, Home choice 11)
- Type of Catheter: Cook catheters 41, Kimal Peel away 10, Surgical inserted Tenckhoff 2
- Catheter Complications minimal
    - Outcomes: Alive 21/49(43 %),
- PIMS I Mean 0.23(PIMS1 0.15 survival; 0.29 died), PIMS II Mean 0.46(PIMS II 0.31 survival; 0.4 died)

Conclusions:
Intravenous fluid has been adapted by adding 50% Dextrose to produce a 'home-made' solution which is safe and effective for use in acute PD. Our survival rate in these particularly sick and very small infants was 43% compared to our standard 60% survival in our conventional acute PD for Paeds AKI group.
Severe infections or electrolyte imbalance were not a significant problem as a result of this adapted PD fluid. This has important relevance for centres in less well-resourced countries across the world where commercially produced PD fluid is not available for management of AKI.

(ETHICS NO: 646/2015)

Title: **PREVALENCE AND DETERMINANTS OF *STAPHYLOCOCCUS AUREUS* NASOPHARYNGEAL CARRIAGE AMONG AFRICAN INFANTS**

Authors: Shima M. Abdulgader[1], Lourens Robberts[1], Mohammed Fadul[2], Sugnet Gardner-Lubbe[3], Heather J Zar[4], and Mark P. Nicol[1, 5, 6]

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[6]National Health Laboratory Service, Groote Schuur Hospital, Cape Town, South Africa

Background:
Data on the prevalence and determinants of *Staphylococcus aureus* nasopharyngeal (NP) carriage during the first year of life in low and middle income countries are lacking.

Methods:
137 mother-infant pairs were enrolled from two clinical sites (Mbekweni and TC Newman) as part of the Drakenstein Child Health Study (DCHS), a longitudinal birth cohort study. We collected NP swabs from 125 mothers and infants at birth and from 137 infants every two weeks for 12 months of life. *S. aureus* was identified using conventional microbiological culture methods. Binomial logistic regression models were used to investigate the association between predictive variables and *S. aureus* NP carriage. The study was approved by the Faculty of Health Sciences, University of Cape Town Human Research Ethics Committee HREC Ref: 741/2103

Results:
Of 3417 NP swabs collected, *S. aureus* was detected in 17% (21/125) of mothers and in 21% (704/3292) of infants Among infants, the NP carriage rate was 2.3% at birth, peaked to 54% at four weeks and declined with increasing age to 6.6% at 1 year. On multivariate analysis male gender (Odds Ratio (OR) 1.25; 95%CI 1.01-1.54), maternal carriage (OR=1.94; 95%CI 1.45-2.60), day care attendance (OR=1.33; 95%CI 1.03-1.71), large family size (≥ 5 individuals) (OR=1.54; 95%CI 1.20-1.97), higher socioeconomic status (OR=1.54; 95%CI 1.21-1.97) or season (spring/summer) (OR=1.61; 95%CI 1.21-2.14) were associated with *S. aureus* NP carriage. In contrast, having a pet (OR 0.77; 95%CI 0.61-0.96) or cigarette smoke exposure from either mothers or households were negatively associated with *S. aureus* carriage. The odds of carrying *S. aureus* changed over time among HIV-exposed or *S. pneumoniae* carrier infants. HIV exposed infants tended to carry *S. aureus* for shorter durations but re-acquire carriage more frequently than HIV-unexposed infants. An inverse association was observed overtime between carriage of *S. aureus* and *S. pneumoniae* during the first year of life.

Conclusion:
A high prevalence of *S. aureus* NP carriage was observed among healthy South African infants especially in the first month of life. Complex interactions between different risk factors are likely to be important in determining prevalence and duration of carriage.

Title: **FEEDING PRACTICES AND HIV EXPOSURE ARE THE PRIMARY DRIVERS OF INFANT FAECAL BACTERIAL PROFILES IN THE DRAKENSTEIN CHILD HEALTH STUDY**

Authors: Shantelle Claassen-Weitz[1]*, Sugnet Gardner-Lubbe[3], Paul Nicol[4], Gerrit Botha[4], Stephanie Mounaud[5], Jyoti Shankar[5], William C Nierman[5], Nicola Mulder[4], Shrish Budree[6], Heather J Zar[2,6,7], Mark P Nicol,[1,2,8] Mamadou Kaba[1,2]

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Objective:
There are few data on the faecal microbiome in early life amongst African infants. We characterized and determined risk factors associated with the faecal bacterial profiles of infants participating in a South African birth cohort study, the Drakenstein Child Health Study (DCHS).

Methods:
We generated bacterial sequences (of the V4 hypervariable region of the 16S ribosomal RNA gene) from faecal (including meconium) specimens collected from 90 mothers and 107 infants at birth, 72 infants at 4-12 weeks, and 36 infants at 20-28 weeks of life enrolled in the DCHS.

Results:
Meconium bacterial profiles [(dominated by Proteobacteria (89%), Actinobacteria (4%) and Firmicutes (2%)] were distinct from those of maternal faeces ((dominated by Firmicutes (66%), Actinobacteria (15%) and Bacteroidetes (5%)). At 4-12 weeks of age, infant faecal bacterial profiles had shifted and were dominated by Actinobacteria (60%), Firmicutes (21%) and Proteobacteria (16%). Bacterial profiles at 20-28 weeks were similar to those at 4-12 weeks, with an increase in Firmicutes (33%). Exclusive breastfeeding was more common for HIV-unexposed infants compared to HIV-exposed infants at birth (99% (76/77) vs. 42% (11/26)), at 4-12 weeks (49% (26/53) vs. 37% (7/19)), and at 20-28 weeks (17% (6/36) vs. 0% (0/10)). More HIV-exposed infants were exclusively formula fed in comparison to HIV-unexposed infants at birth (58% (15/26) vs 1% (1/77)), at 4-12 weeks (53% (10/19) vs 2% (1/53)), and at 20-28 weeks (70% (7/10) vs 0% (0/26)). HIV-exposed infants had significantly higher faecal bacterial diversities at 4-12 ($p = 0.026$) and 20-28 weeks ($p = 0.002$) of life. Infants exclusively formula-fed up until 4-12 weeks had higher bacterial diversity when compared to infants exclusively breast-fed or mixed-fed ($p = 0.024$). HIV-exposed infants had higher proportions of the genus *Weissella* and lower proportions of *Bifidobacterium* at 20-28 weeks of life compared to HIV-unexposed infants.

Conclusions:
The bacterial community of meconium is distinct from that found in mothers' faeces. Early life feeding practices and HIV exposure were potential drivers of infant faecal bacterial profiles. *Bifidobacterium*, present in lower abundance among formula-fed or HIV-exposed infants in our study, has previously been shown to downregulate the expression of inflammation-related genes with potential impact on child health.

Ethics approval: This study (585/2015), and the DCHS (401/2009), received ethical approval from the Faculty of Health Sciences, Human Research Ethics Committee (HREC) of the University of Cape Town, South Africa.

Previous presentations at UCT Department of Paediatrics and Child Health Research Days:
This is new research to be presented for the first time at the UCT Department of Paediatrics and Child Health Research Days.

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Title: **EARLY-LIFE EXPOSURE TO INDOOR AIR POLLUTION OR TOBACCO SMOKE AND LOWER RESPIRATORY TRACT ILLNESS AND WHEEZING IN AFRICAN INFANTS**

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Background and Objectives:
Indoor air pollution (IAP) and environmental tobacco smoke (ETS) are associated with lower respiratory tract illness (LRTI) or wheezing in children. However, the impact of the timing of exposures, specifically antenatal versus postnatal nor the impact of alternate fuel sources such as volatile organic compounds, increasingly used globally, have not been well studied. We longitudinally investigated the impact of antenatal or postnatal IAP and ETS on LRTI or wheezing prevalence and severity in African infants.

Methods:
Mother–infant pairs enrolled in a South African birth cohort study were followed through infancy for LRTI or wheezing illness. Exposure to IAP (particulate matter, nitrogen dioxide/sulphur dioxide, carbon monoxide and volatile organic compounds, benzene and toluene) was measured using devices placed in homes, antenatally and postnatally, ETS was longitudinally measured by maternal self-report and by urine cotinine measures. Multivariate logistic and Poisson regressions were done.

Findings:
Of 1065 infants, 524 episodes of LRTI occurred with a wheezing prevalence of 0·23 (95% CI 0·21 - 0·26) episodes per child year. Exposures associated with LRTI were antenatal maternal smoking [IR 1·62 (95% CI 1·14 -2·30)] or particulate matter (PM_{10}) [IR 1·43 (95% CI 1·06- 1·95)]. Sub-analyses of LRTI requiring hospitalization (n=245) and supplemental oxygen (n=244) found antenatal toluene increased the risk of LRTI-associated hospitalization (five-fold), OR 5·13 (95% CI 1·43-18·36) and need for supplemental oxygen (thirteen-fold), OR 13·21 (95% CI 1·96-89·16). Wheezing illness was associated with antenatal maternal smoking [IR 2·09 (95% CI 1·54-2·84)], maternal passive smoke exposure [IR 1·70 (95% CI 1·25-2·31)] while postnatally, maternal smoking IR 1·27 (95% CI 1·03 – 1·56) and any household member smoking IR 1·55 (95% CI 1·17 –2·06) was associated with wheezing.

Conclusion:
Antenatal exposures were the predominant risk factors associated with LRTI or wheezing illness. Toluene was a novel exposure associated with severe LRTI.

Funding: Bill & Melinda Gates Foundation, Discovery Foundation, South African Thoracic Society AstraZeneca Respiratory Fellowship, Medical Research Council South Africa, National Research Foundation South Africa, and CIDRI Clinical Fellowship.

Title: **DIAGNOSTIC PERFORMANCE OF LUNG ULTRASOUND COMPARED WITH CHEST RADIOGRAPHS FOR PNEUMONIA IN CHILDREN IN THE DRAKENSTEIN CHILD HEALTH STUDY**

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Introduction:
Chest radiography (CXR) is the first-line imaging modality for suspected pneumonia in children. However, CXR features of pneumonia have moderate sensitivity and specificity and poor inter-rater reliability (IRR) and expose children to ionising radiation. Lung ultrasound (LUS) may be a radiation-free, lower-cost alternative for the diagnosis of pneumonia.

Objectives:
To compare the diagnostic performance of LUS and CXR in children with suspected pneumonia.

Methods:
LUS was performed on 103 children in the Drakenstein Child Health Study who presented with clinical features consistent with pneumonia (World Health Organization case definition) and who received a CXR as part of routine care. IRR between a general practitioner and a paediatric radiologist for the interpretation of LUS findings for pneumonia were compared with CXR interpretation by two specialist paediatricians. IRR of different LUS features was also compared.

Results:
The study included 72 hospitalised and 31 non-hospitalised pneumonia cases with a median (IQR) age of 7.3 (2.6-18.3) months. The general practitioner and paediatric radiologist reported LUS findings consistent with pneumonia in 58% (*n*=60) v. 52% (*n*=54) of cases, respectively. The overall agreement on LUS findings was substantial (kappa=0.60) compared with poor agreement on CXR (kappa=0.25). On LUS, there was better agreement for consolidation (kappa=0.69) and for a normal scan (kappa=0.65) than for interstitial syndrome (kappa=0.43).

Conclusion:
LUS demonstrated better IRR than CXR for detecting features of pneumonia in children. Consolidation is a more reliable sonographic sign of pneumonia than interstitial syndrome. LUS may be preferable to CXR for the diagnosis of pneumonia in children.

Title: **LOW LUNG FUNCTION AT SIX WEEKS OF AGE IN HEALTHY SOUTH AFRICAN INFANTS PREDICTS LOWER RESPIRATORY TRACT ILLNESS DURING THE FIRST YEAR OF LIFE**

Authors: Diane Gray, Dorottya Czovek, Lauren McMillan, Lidija Turkovic, Jacobus Stadler, Aneesa Vanker, Bence Radics, Zoltan Gingl, Graham L Hall, Peter D Sly, Zoltan Hantos, Heather J Zar

Background:
Lower respiratory tract illness (LRTI) is the leading cause of mortality and morbidity in children. LRTI in early life lowers lung function. It is unclear whether pre-existing low lung function contributes to risk of developing LRTI.

Aim:
To investigate whether lung function, in particular that derived from the within-breath FOT, performed shortly after birth was able to identify apparently healthy infants at risk of LRTI in the first year of life.

Methods:
Lung function was measured with the multiple breath washout technique, tidal breathing analysis, exhaled nitric-oxide and the novel within-breath forced oscillation technique (FOT), in six-week old infants in a South African birth cohort (Drakenstein Child Health Study). Subsequent LRTI during the first year of life were confirmed by study staff. The association between baseline lung function and LRTI was assessed with logistic regression. Optimal cut-offs and odds ratios (ORs) were determined in the relevant measures.

Results:
Of the 627 healthy infants who had successful lung function testing, 161(24%) had 238 LRTI episodes during the first year of life.

Table: Demographics and lung function in infants with and without respiratory tract infection

	No LRTI (n=466)	Any LRTI (n=161)	p-value*
Gestational age, mo	39 (37; 40)	39 (38; 40)	0.633
Gender, male n(%)	217 (47)	98 (61)	0.002
Length z-score	-0.73 (-1.7; 0.1)	-0.88 (-1.9; 0.04)	0.052
Maternal antenatal smoking: Active (n, %) Passive (n, %) No exposure (n, %)	 134 (30%) 202 (46%) 106 (24%)	 42 (37%) 64 (42%) 26 (17%)	 0.089 0.629 0.361
Maternal HIV infection (n, %)	96 (19%)	36 (22%)	0.632
t_{PTEF}/t_E %	38.7 (30.1; 46.2)	35.1 (27.0; 35.5)	0.053
X_{exp} (hPa.s/L)	-8.8 (-15.0; -5.0)	-12.6 (-19.0; -6.9)	<0.001
X_{insp} (hPa.s/L)	-5.1 (-9.0; -1.0)	-5.2 (-10.0; -1.9)	0.405
ΔR (hPa.s/L)	4.43 (0.7; 8.1)	5.6 (1.6; 11.2)	0.007
ΔX (hPa.s/L)	-1.0 (-4.7; 1.4)	-3.0 (-7.5; -0.53)	<0.001
*adjusted for gestational age, size and gender; continuous variable reported as median and interquartile range			

FOT measures were associated with subsequent LRTI: expiratory reactance $X_{exp,}$ volume dependence of resistance (ΔR) and reactance (ΔX). These measures and expiratory flow ratios were associated with LRTI with wheeze. The predictive value was stronger if LRTI was recurrent (n=50, 31%): highest OR=2.5, for ΔX; required hospitalisation (n=38, 16%): OR=5.4, for ΔR; or was associated with wheeze (n=87, 37%): OR=3.9, ΔX. An increased t_{PTEF}/t_E ratio increased the odds (OR:2.6) of LRTI-associated wheezing.

Conclusion:
Low lung function as reflected by a within-breath impedance measurement shortly after birth increases risk of LRTI, wheezing and severe LRTI in infancy. This new technique provides a safe and useful assessment of lung function in unsedated infants that can be used longitudinally.

Title: **AMBULATORY AND HOSPITALISED PNEUMONIA IN THE FIRST 2 YEARS OF LIFE IN A SOUTH AFRICAN BIRTH COHORT: THE DRAKENSTEIN CHILD HEALTH STUDY**

Authors: David M le Roux[1,2], Mark P Nicol[3], Landon Myer[4], Heather J Zar[1]

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Background:
Childhood pneumonia causes substantial morbidity and long term morbidity later in life. This study describes incidence and risk factors for ambulatory and hospitalised pneumonia in the first 2 years of life in children enrolled in a South African birth cohort.

Methods:
Pregnant women living in a peri-urban area of South Africa were enrolled in a birth cohort, the Drakenstein Child Health Study. Mother-infant pairs were followed for 2 years; data on risk factors and respiratory symptoms were collected. Ambulatory and hospitalised pneumonia episodes were documented. Pneumonia incidence rate ratios (IRR) were calculated using Poisson regression.

Results:
From May 2012 till February 2017, 1143 children were followed for 2048.6 child-years. Maternal smoking (23%) and HIV infection (22%) were common. There were 795 pneumonia cases in the first 2 years of life, 621 (78%) ambulatory and 174 (22%) requiring hospitalization. Most cases occurred in the first year: 400 (64%) of the ambulatory and 138 (79%) of the hospitalized events. The 795 cases occurred in 429 children (38%); 189 children (17%) had a second and 87 (8%) had a third pneumonia. Incidence was high in the first year of life (0.51 episodes per child year, e/cy) and 0.25 e/cy in the second year. Increased incidence was observed in babies born pre term (IRR 1.50, 95% CI 1.18 – 1.91), of low birth weight (IRR 1.70, 95% CI 1.32 – 2.18) and children with wasting (weight for length Z score of less than -2; IRR 1.41, 95% CI 1.11 – 1.79). Children hospitalised with pneumonia were more likely to be younger (less than 2 months), pre-term or low birth weight, have severe disease, hypoxia or associated diarrhoea, compared to ambulatory cases. HIV exposed uninfected children had increased incidence of hospitalised pneumonia, IRR 1.46 (95% CI 0.87 – 2.44). Once adjusted for confounders, antenatal maternal antiretroviral therapy (ART) eliminated the effect of HIV exposure on incidence of hospitalized pneumonia.

Conclusion:
Pneumonia incidence was high in the first year of life; wasting and HIV exposure were strongly associated with pneumonia. Improved nutrition and maternal ART may reduce pneumonia incidence.

Funding: Bill and Melinda Gates Foundation, grant number OPP1017641; Medical Research Council; South African Thoracic Society; Federation of Infectious Diseases Societies of South Africa; UCT PhD research associateship; UCT HREC 401/2009 and 651/2013

Title: **CHARACTERIZING ANTIBIOTIC-RESISTANT PNEUMOCOCCI IN THE NASOPHARYNX OF HEALTHY SOUTH AFRICAN INFANTS USING SHOTGUN SEQUENCING AND CONVENTIONAL TYPING**

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Introduction:
The increased prevalence of antibiotic-resistant *Streptococcus pneumoniae* is of public health concern. *S. pneumoniae* is one of the leading causes of death in infants. We longitudinally investigated antibiotic-resistant *S. pneumoniae* in the nasopharynx of healthy infants in the Drakenstein Child Health Study, using conventional and shotgun sequencing methods.

Methods:
Nasopharyngeal (NP) swabs were collected fortnightly from birth through the first year of life, from 137 infants. Infants received 3 doses of 13-valent pneumococcal conjugate vaccine (PCV13). *S. pneumoniae* isolates were serotyped using sequetyping and Quellung. Antibiotic susceptibility profiles were determined using disc diffusion and E-test. Metagenomic shotgun sequencing was performed on a subset of 200 NP samples from 23 infants, selected on the basis of changing serotype or antibiogram over time.

Results:
S. pneumoniae was isolated from 54% (1809/3331) NP swabs. After correcting for repeated acquisition of the same serotype with a unique antibiogram (33%; 591/1809), non-susceptibility to penicillin G, erythromycin, and cotrimoxazole was found in 26% (125/591), 20% (120/591), and 42% (250/591) of the isolates respectively. Multidrug resistance (MDR) was observed in 11% (67/591) of the *S. pneumoniae* with vaccine types 9V (n= 5), 19F (n= 5), and non-vaccine type 15B/C (n= 9), being predominant serotypes. We found a 68% (136/200) concordance between shotgun sequencing and conventional serotyping, with co-colonization by multiple pneumococcal serotypes identified in 23 samples by shotgun sequencing. We detected 26 different sequence types (including 4 novel ST), predominantly ST8687 and ST2068 (ST2068 not previously described in Africa) and 31 different antibiotic resistance genes by shotgun sequencing.

Conclusion:
MDR was noted in a small proportion of isolates. Shotgun sequencing is a valuable technique for detailed evaluation of the pneumococcal component of the NP microbiome.

The study was approved by the Faculty of Health Sciences (FHS) Human Research Ethics Committee (HREC) of the University of Cape Town, South Africa (HREC reference number: 235/2016).

Title: **LONGITUDINAL CHANGES IN LUNG FUNCTION IN HIV- INFECTED ADOLESCENTS ON ANTIRETROVIRAL THERAPY IN CAPE TOWN, SOUTH AFRICA**

Authors: Githinji L[1], Gray D[1], Hlengwa[1] S, Machemedze T[1], Myer L[2], Zar HJ[1]

Affiliation: [1] Department of Paediatrics and Child Health, Red Cross Children's Hospital and MRC Unit on Child and Adolescent Health, University of Cape Town, South Africa [2] Division of Epidemiology & Biostatistics, School of Public Health & Family Medicine, University of Cape Town

Background:
Over 90% of HIV-infected children live in Sub-Saharan Africa. Despite increased access to antiretroviral therapy, respiratory illness remains common in HIV-infected youth. There is limited information on progression of lung function in HIV-infected adolescents on antiretroviral therapy.

Objective:
We aimed to investigate progression of lung function over 2 years in HIV-infected adolescents on antiretroviral therapy in a prospective cohort, the Cape Town Adolescent Anti-retroviral cohort (CTAAC).

Methods:
HIV-infected adolescents aged 9-14 years, with at least 6 months of antiretroviral therapy, enrolled on CTAAC, underwent lung function testing. Spirometry and bronchodilator testing was done at enrolment and annually for two years. Healthy HIV-uninfected, age, sex and ethnically matched controls were also tested. Linear mixed models were used to compute longitudinal changes in lung function outcomes.

Results:
Four hundred and twenty eight HIV-infected adolescents and 90 HIV-uninfected were tested at baseline and at 24 months. Mean (SD) age was 12.0 (1.6) years and 50.4% male. Median (IQR) viral load and CD4 count at baseline were 2.2 (1.6-3.3) log copies and 731 (580-959) cells/mm^3 respectively. HIV-infected adolescents had on average 0.51 lower z-FEV_1 over two years compared to HIV-uninfected youth, p<0.001, but there was no difference in change in z-FEV_1 between the two groups over time, p=0.575. Obstructive or mixed lung function patterns were more common in HIV-infected adolescents at 24 months.

		HIV-infected **(N=428**)	HIV-uninfected **(N=90)**	
	Time	Mean (SD)	Mean (SD)	p-value
z-FVC	baseline	-1.08 (1.32)	-0.88 (1.08)	0.175
	24 months	-0.69 (1.19)	-0.29 (0.96)	0.003
z-FEV_1	baseline	-0.98 (1.33)	-0.50 (1.03)	0.001
	24 months	-0.80 (1.31)	-0.27 (0.95)	0.000
Change z-FEV_1 ($fev1_{t5}$-$fev1_{t1}$)		0.18 (0.89)	0.24 (0.83)	0.575
N (%) restrictive spirometry	baseline	105 (24.53)	20 (22.22)	0.641
	24 moths	60 (14.02)	6 (6.67)	0.057
N (%) obstructive spirometry	baseline	41 (9.58)	4 (4.44)	0.116
	24 moths	59 (13.79)	5 (5.56)	0.031
N (%) mixed spirometry	baseline	18 (4.21)	0 (0.00)	0.048
	24 moths	25 (5.84)	0 (0.00)	0.019
		N = 408	**N = 89**	
N (%) BDR>12% in FEV_1	baseline	67 (16.42)	9 (10.11)	0.134
	24 moths	24 (5.97)	4 (4.55)	0.602

p values ttest, z-FVC forced vital capacity z-score, z-FEV_1 forced expiratory volume in 1 sec z-score, BDR bronchodilator responsiveness FEV_1 change>12%, obstructive spirometry=FEV_1/FVC<lower limit of normal using African-American reference values, restrictive spirometry= FVC<LLN and FEV_1/FVC≥lower limit of normal; mixed spirometry =FEV_1<LLN and FVC<LLN and FEV_1/FVC<LLN

Conclusion:
HIV-infected adolescents had significantly lower lung function than HIV-uninfected at all time points. Lung function tracked similarly over 2 years between groups, suggesting no catch up growth nor lung function deterioration over time.

Funding: NIH R01HD074051, MRC SA

Title: **THE IMPACT OF PRENATAL METHAMPHETAMINE EXPOSURE ON ANTERIOR CINGULATE CORTEX NEUROMETABOLITE CONCENTRATIONS IN CHILDREN: AGES 6 AND 8 YEARS OLD**

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Background:
The impact of prenatal methamphetamine exposure (PME) on neurodevelopment of children is of growing concern, as methamphetamine (MA) has been shown to alter cortical development, including the anterior cingulate cortex (ACC). This study investigated the impact of PME on proton magnetic resonance spectroscopy (1H-MRS) neurometabolite concentrations within the ACC of PME children at age 6 years then at 8 years old, compared with healthy socio-demographically matched controls (CON).

Methods:
Children with PME (n=9) and CON (n=7) underwent single-voxel 1H-MRS (TR 2000ms, TE 30ms) of the ACC, absolute neurometabolite concentrations are reported. 1H-MRS was performed at 6 years of age (PME: 77.67±4.95mnths; CON: 76.29±3.90mnths), and 8 years of age (PME: 94.78±5.97mnths; CON: 96.86±4.85mnths).

Results:
Lower concentrations of n-acetyl-aspartate (NAA) were found in PME children at age 8 when compared with PME children at age 6 years old. Glycerophosphocholine with phosphocholine (GPC+PCh) and NAA correlated with age of the PME children at age 6 years old and with CON group at age 8 years old, these relationships were not evident in PME children at 8 years old.

Conclusion:
This study reports ACC neurometabolite differences in PME children at age 8 years old, however these differences are not apparent at 6 years old. These differences observed in the PME group suggest changes in developmental neuronal trajectory with increasing age. In order to investigate the potential mechanisms underlying these differences found in PME children at 8 years old further longitudinal studies are required.

Title: **RITUXIMAB USE IN PAEDIATRIC MESANGIOPROLIFERATIVE NEPHROTIC SYNDROME**

Authors: Coetzee AC, Reddy D, McCulloch M, Nourse P

Background:
Nephrotic Syndrome has an incidence of 1-3 per 100 000 children under the age of 16 years according to the 2012 kidney disease: improving global outcomes (KDIGO), with 80-90% responding to first line steroid therapy.
Histologically 80% of idiopathic nephrotic syndrome is due to minimal change glomerulonephritis, however the incidence of mesangioproliferative glomerulonephritis varies depending on geographical and ethnic differences. A review of biopsies at our institution showed that half were mesangioproliferative glomerulonephritis.
In patients with 'difficult to control' nephrotic syndrome, Rituximab have been shown to induce remission and allow steroid free periods.

Objective:
To determine the effectiveness of Rituximab in mesangioproliferative glomerulonephritis in a paediatric population.

Methods:
A retrospective cohort review of nephrotic database was conducted to identify patients with histological diagnosis of mesangioproliferative glomerulonephritis and who had received Rituximab. Data was collected with regards to dosing, adverse effects, CD19% reduction and relapse rate. Data on the immunosuppressive medication before and after Rituximab was also collected.

Results:
Of the 110 biopsied patients, 9 had received rituximab, with 5 having mesangioproliferative glomerulonephritis. 1 was excluded due to inadequate records. All 4 had been on a range of immunosuppressive agents prior to Rituximab administration. A mean Rituximab dose of 490mg/m^2 was administered without any adverse effects and effective CD19% suppression. Rituximab administration improved the relapse rate and allowed weaning off steroids in 3 of the 4 patients.

Conclusion:
In our geographic area mesangioproliferative glomerulonephritis represents most renal biopsy histological diagnosis. Rituximab is an effective medication in the treatment of difficult steroid sensitive and steroid resistant nephrotic syndrome.

Title: **VARIANTS IDENTIFIED IN FAMILIES WITH CEREBRAL CAVERNOUS MALFORMATION (CCM)**

Presenter: Ilse Crous

Introduction:
Cerebral cavernous malformations (CCM) are vascular malformations in the brain and spinal cord that have a raspberry like appearance. It consists of abnormally dilated capillary channels with a single layer of endothelium. The diameter can range from a few mm to several cm. It can increase or decrease in size and number over time. Cutaneous vascular lesions are found in approximately 9% of people with Familial cerebral cavernous malformations (FCCM). Retinal vascular lesions are found in about 5% of people with FCCM. Up to 50 % of individuals with Familial CCM can remain symptom free throughout their lives.

Objectives:
We report on two families, both with a significant family history of cerebral cavernous malformations (CCM). The genetic cause has not been established and the families attended with the hope of undergoing genetic testing and having a pathogenic variant identified.

Methods:
After counselling, a saliva sample was collected from both index patients and sent to Invitae for CCM panel testing. The panel includes three genes that are associated with familial CCM namely *KRIT1*, *PDCD10* and *CCM2*.
Family 1: We report on a 7-year-old female. She presented with a vascular skin lesion on the dorsum of right foot and symptoms of micropsia. A MRI identified multiple cerebral cavernomas. The patient's mother and two maternal uncles have been diagnosed previously by means of MRI modality and the parents are concerned about their children.
Results Patient 1: The patient was found to carry a heterozygous, pathogenic variant: *KRIT1*, Exon 14, c.1267C>T (p.Arg423*).
Family 2: The second case consist of a six year old male, who initially presented with headaches and vomiting. Symptoms progressed to weakness and sensory loss in right arm and hand. Upon hospital admission he had a single tonic clonic seizure. Surgery was commenced because of severe raised intracranial pressure. A left sided paraventricular bleed due to cerebral cavernous malformation was located. The father had two incidents in 2005 and 2015, which presented in the same manner with right arm weakness and sensory loss and was treated conservatively. The paternal Aunt was also diagnosed with CCM in 2015.
Results Patient 2: A Variant of Uncertain Significance was identified in the *CCM2* gene. This heterozygous variant was found in Exon 6, c.635T>C (p.Leu212Pro).

Conclusion:
Identifying the genetic cause has implications for the patients and her families. Recognition of a pathogenic variant allowed us the ability to offer testing to rest of family 1, including 3 siblings. As the *KRIT* gene is associated with autosomal dominant CCM, the patient's siblings are at 50% risk of having inherited this variant. The management of patients with CCM is complex as most lesions remain benign but the risks of bleeding, seizures and neurological deficits are significant (>30%). The counselling issues in these cases centred on the parent's need for information, the issue of testing the siblings and management of the child and the family. These issues will be unpacked and further management of the cases will be discussed.

Title: **RETROSPECTIVE ANALYSIS OF ABANDONED LIVE BIRTHS, STILLBIRTHS AND NON-VIABLE FOETUSES ADMITTED TO SALT RIVER MORTUARY, CAPE TOWN**

Authors: Chanté du Toit, Lorna J Martin and Laura J Heathfield

Affiliation: Division of Forensic Medicine and Toxicology, Department of Pathology, Faculty of Health Sciences, University of Cape Town, Anzio Road, Observatory, 7925, South Africa

Background:
Every year, a significant number of abandoned foetal and new-born remains are admitted to Salt River Mortuary (SRM) for post-mortem examination. These cases include non-viable foetuses and stillbirths (natural deaths), as well as abandoned live births (unnatural deaths); the latter having possible legal or criminal implications. The high rates and the dearth of literature published in South Africa prompted a retrospective review of abandoned neonates admitted to SRM.

Aim and objectives:
The aim of this study was to assess abandoned neonates admitted to SRM over a 5-year period. As such, the objectives were to retrospectively analyse data for abandoned neonates in order to describe the profile and assess the scope of the post-mortem investigation of these cases, and determine the prosecution rate of abandoned live births.

Methods:
Medico-legal case files concerning non-viable foetuses, stillbirths and concealment of birth cases at SRM between 1 January 2012 and 31 December 2016 were utilised to collect demographic details, scene information and post-mortem findings. Cases identified as abandoned live births were followed up with the South African Police Service to determine the prosecution rate. Data were analysed using SPSS Statistics version 24.

Results:
A total of 249 of abandoned neonates were admitted to SRM over a 5-year period (44-56 cases per year). The mass, length and gestational age ranged between 10-4400g, 18-600mm, and 7 weeks to term, respectively. Of these cases, the sex could not be determined in 29 (11.6%) cases due to post-mortem mutilation (n=3), undifferentiated genitalia (n=3) or no reason given (n=22). Natural deaths accounted for the majority (70.3%) of the cases, with 66.9% and 29.1% of these cases being non-viable foetuses and stillbirths, respectively. The cause of death could not be determined in 51 (20.5%) cases, and was attributed to the presence of decomposition in 19 (37.3%) cases, with histology only performed in 2 (10.5%) of these cases. Of the deaths determined to be due to unnatural causes (n=23, 9.2%), one case was prosecuted, and for the remainder of the cases, the court status was equally distributed between 'case closed' and 'under investigation' (11 cases each, 47.8%). In 17 out of 21 instances of either unnatural or undetermined cause of death, the case was closed due to the fact that the identity of the biological mother could never be established. DNA analysis was only performed in 12 of these 17 cases.

Conclusions:
While the concern of abandoned neonates is not unique to South Africa, we have seemingly higher rates compared to other countries. Despite the majority of the cases being natural deaths, the cause of death frequently remains 'undetermined' in these cases. The presence of decomposition often hinders further post-mortem investigation. Furthermore, the suspicion that the prosecution rate of abandoned live births is extremely low is corroborated by this study.

Ethics: This study received approval from the University of Cape Town, Faculty of Health Science, Human Research Ethics Committee (HREC REF: 061/2017).

Title: **INSPIRATORY MUSCLE TRAINING FOR CHILDREN AND ADOLESCENTS WITH NEUROMUSCULAR DISEASES: A SYSTEMATIC REVIEW**

Authors: Anri Human[1,2], MPhysT; Lieselotte Corten[2], PhD; Jennifer Jelsma[2], PhD; Brenda Morrow[3], PhD

Affiliation: [1]School of Health Care Sciences (Physiotherapy department), Sefako Makgatho Health Sciences University; [2]Department of Health and Rehabilitation Sciences (Division Physiotherapy), University of Cape Town; [3]Department of Paediatrics and Child Health, University of Cape Town.

Background:
Children with neuromuscular diseases (NMD) are at risk of morbidity and mortality due to respiratory compromise, caused primarily by diaphragmatic and intercostal muscle weakness. Inspiratory muscle weakness can lead to decreased lung volumes; altered and ineffective breathing; decreased thoracic and shoulder mobility, chest expansion and alveolar ventilation; poor secretion clearance and ultimately respiratory failure. The use of inspiratory muscle training (IMT) to improve or preserve respiratory function in patients with NMDs remains controversial.

Objectives:
To determine the safety of IMT and its effect on morbidity, adverse events, muscle strength and endurance, pulmonary function, dyspnoea and health-related quality of life (HRQoL), in children and adolescents with NMD.

Methods:
The Cochrane methodology for systematic reviews was followed (Prospero CRD42014013875). Fifteen online databases were searched for published and on-going studies, using pre-specified search strategies. Randomised, quasi-randomised, cross-over and clinical controlled trials assessing the use of an external IMT device compared to no, sham/placebo, or alternative IMT intervention in children aged five to 18 years with NMD were included. Data from included studies were extracted using a pre-structured data extraction form. The methodological quality and risk of bias of included studies were independently assessed using a standardised tool. Data were analysed using RevMan software (version 5.2).

Results:
Seven studies (n=168) were included, the majority of which included males with Duchenne Muscular Dystrophy. The intensity, repetitions, frequency, rest intervals and duration of IMT differed amongst studies, but most used threshold IMT devices with mouthpieces over a medium to long-term period (3-6 months). Six studies reported no significant improvement in pulmonary function following IMT. Two studies reported significant improvement in inspiratory muscle endurance and four studies reported significantly greater improvement in inspiratory muscle strength in experimental groups. The latter was confirmed in a meta-analysis of two comparable studies for mean maximum inspiratory muscle strength (Pimax/MIP) in cmH_2O (overall effect $p< 0.0001$). Other outcome measures could not be pooled due to heterogeneity.

Conclusions:
There is no clear evidence for or against the use of IMT in children and adolescents with NMD, despite some improvements in inspiratory muscle strength (Pimax) and individual endurance. Improvement in Pimax could be attributed to a "learning effect" due to training with a threshold device. There is currently no consensus regarding optimal respiratory muscle training devices, frequency or dosage in patients with NMD. Owing to the limited number of included studies; small sample sizes; data heterogeneity; and risk of bias amongst included studies; large sample randomised controlled trials are needed to determine safety and efficacy of IMT in paediatric and adolescent patients with NMD.

Ethics approval: Human Research Ethics Committee (UCT): 513/2015
This research has been presented at the World Confederation for Physical Therapy Congress, 2017.

Title: **RESPIRATORY CARE IN CHILDREN AND ADOLESCENTS WITH NEUROMUSCULAR DISEASES: A SOUTH AFRICAN PERSPECTIVE**

Authors: Anri Human[1,2], MPhysT; Lieselotte Corten[2], PhD; Jennifer Jelsma[2], PhD; Brenda Morrow[3], PhD

Affiliation: [1]School of Health Care Sciences (Physiotherapy department), Sefako Makgatho Health Sciences University; [2]Department of Health and Rehabilitation Sciences (Division Physiotherapy), University of Cape Town; [3]Department of Paediatrics and Child Health, University of Cape Town

Background:
Airway clearance therapy is a recommended part of the respiratory care regimen for children with neuromuscular diseases (NMD) presenting with respiratory muscle weakness and a weak cough.

Objectives:
To explore South African physiotherapists' perceptions, experience and prescription of respiratory care modalities in non-ventilated paediatric and adolescent patients with NMD.

Methods:
A cross-sectional descriptive research study design was implemented and a non-probability purposive sampling frame was used. A self-constructed, content validated, questionnaire was distributed to 475 physiotherapists with a special interest or expertise in the field of respiratory care and/or paediatrics, using an online survey platform.

Results:
The overall response rate was 74 (16%). Of these respondents, 59 (80%) were eligible because they have previously worked with patients with NMD. The majority of participants worked in private practice and/or hospital wards and had less than five years postgraduate clinical experience. The most frequently chosen techniques used for acute general respiratory care were supplemental oxygen delivery and 24-hour postural management. Vibrations, positioning and breathing exercises were favoured for mobilising secretions and manually assisted cough was strongly supported for cough augmentation. The majority either were not aware of mechanical insufflation-exsufflation as an alternative cough augmentation technique or was aware of the device, but had never used it before. For chronic management, the majority of participants supported inspiratory muscle training and breathing exercises as part of respiratory muscle training and lung compliance exercises. However, 50% of participants were unsure about the use of breath stacking, manual inflation, or glosso-pharyngeal breathing for chronic management. Nebulisation and positioning were favoured as secretion mobilisation techniques whilst manually assisted cough was strongly supported for airway clearance and cough assistance. Further, 24-hour postural management and non-invasive ventilation were mostly used for respiratory support. Only six (10%) participants had recently treated children and adolescents with NMD. They used vibrations, adapted postural drainage, positioning and breathing exercises as part of acute respiratory management. Adapted postural drainage, positioning, breathing exercises and autogenic drainage were mostly used for chronic management. Mechanical insufflation-exsufflation was not used by any participant in the past six months.

Conclusions:
South African physiotherapists were generally aware of international clinical guidelines for the respiratory management of paediatric patients with NMD, but traditional chest physiotherapy techniques are still favoured. Internationally endorsed airway clearance techniques such as breath stacking, manual inflation, glossopharyngeal breathing and mechanical insufflation-exsufflation are infrequently used. South African physiotherapists appear to have limited exposure and experience in managing paediatric and adolescent patients with NMD.

Ethics approval: Human Research Ethics Committee (UCT): 513/2015
This research has been presented at the World Confederation for Physical Therapy Congress, 2017

Title: **CATHCHAT AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL: A NOVEL LIVE ONLINE TEACHING AND LEARNING PLATFORM FOR INTERVENTAIONL PAEDIATRIC CARDIAC CATHETERISATION**

Authors: Rik De Decker, Andre Gouws, Jerome Corns, John Lawrenson

Affiliation: Department of Paediatrics and Child Health, University of Cape Town

Background:
In Africa, paediatric interventional catheterisation skills can only be gained by undergoing fellowship training overseas, or by attending costly international congresses. Consequently, there is a dire shortage of trained interventional cardiologists and limited opportunities for such training exist.

There is also a shortage of facilities for congenital heart *surgery* - the majority of affected children will receive no treatment and die. Interventional cardiac catheterisation, however, holds promise to begin to address this need, since surgical or intensive care facilities are usually not required for the interventional management of common, "simpler" congenital heart defects, e.g. ASDs, PDAs.

Methods:
CATHCHAT, developed at the RCWMCH is a system whereby interventional cardiac catheterisation procedures can be streamed live via the Internet. Local and international audiences log in to witness the procedures in real time and are able to interact directly with the operators in the cath lab. The audience is able to follow the procedure in high-definition, step-by-step detail, cost-free.

Results:
CATHCHAT has been growing over the past 3 years, and has broadcast more than 80 live cases to date. All paediatric cardiac centres in South Africa, as well as many centres in Africa, Australia, India and Europe have logged in to observe, and comment on procedures. Its power is that renowned interventional experts also log in and advise the Cathlab operators live while the procedure is being performed. The logged-in audience may then witness the procedure, and learn from observing our experience. This *triangular* model of "telemedicine" is unique.

Conclusion:
CATHCHAT is stimulating the growth of paediatric interventional cardiac catheterisation capacity in Africa. A research module to assess its potential impact is currently under development.

Title: **CARDIAC DISEASE IN HUMAN IMMUNODEFICIENCY VIRUS INFECTED ADOLESCENTS ON HIGHLY ACTIVE ANTIRETROVIRAL THERAPY**

Authors: Mahtab S, Lawrenson J, Zuhlke L, Jamieson-Luff N, Asafu-Agyei NA, Myer L, Zar HJ

Background:
Prior to the availability of antiretroviral therapy (ART), cardiac disease was common amongst children infected with human immunodeficiency virus (HIV). Few studies have explored cardiac outcomes in perinatally HIV-infected (PHIV+) adolescents on highly active ART (HAART).

Objective:
The aim of this study was to investigate structural cardiac abnormalities in HIV-infected adolescents well established on HAART compared to age matched controls.

Methods:
Echocardiograms were performed on PHIV+ adolescents and age matched controls enrolled in the Cape Town Adolescent Antiretroviral cohort (CTAAC). Adolescents were eligible if they were aged between 9-14 years and had been on ART for at least 6 months. Lipid profile [total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL) and low-density lipoprotein cholesterol (LDL)] were performed on fasting serum samples. In the HIV-infected group, plasma HIV-1 viral load (VL) and CD4 T-lymphocyte (CD4) counts were done. Structural dimension for echo parameters were adjusted by using z-scores according to body surface area (BSA). For PHIV+ adolescents multivariate logistic models were used to examine the adjusted association between echo measures (left ventricular (LV) hypertrophy, LV diastolic dysfunction and right ventricular (RV) systolic dysfunction) and HIV related and usual cardiovascular risk factors.

Results:
There were 474 PHIV+ adolescents (median age, 12 years; 51% male; mean age at ART initiation 5 years, SD ±3.5) and 109 controls (median age, 11.8 years; 45% male) enrolled. Mean duration on ART was 7.0 (SD ±3.0) years with 169 (35.7%) starting ART between 6-14 years of age. Almost a quarter (22.2%) were WHO HIV stage IV. Median TC (4.1 vs 3.8 mmol/L, p<0.001), LDL-C (2.2 vs 2.0 mmol/L, p=0.013), and TG (0.9 vs 0.7 mmol/L, p<0.001) were higher in PHIV+ adolescents.

PHIV+ adolescents had higher mean z-scores for LV internal dimension at the end of diastole (-0.16 vs -0.49, p=<0.01), LV posterior wall thickness at the end of systole (-0.45 vs -0.65, p=0.01) and thickness of inter-ventricular septum at the end of systole (0.7 vs 0.6, p=0.04) but lower RV internal dimension at end systole (0.24 vs 0.43, p=0.01) compared to controls. Later initiation of ART was associated with LV hypertrophy, those who started ART between age 6-14 years were at increased risk (OR 2.9, p=0.012) of having LV hypertrophy compared to those started ART earlier. PHIV+ adolescents with WHO HIV stage IV were at increased risk (OR 2.14, p=0.051) of having LV diastolic dysfunction compared to those with less advanced clinical disease (p=0.051).

Conclusion:
No major differences were found in cardiac abnormalities in this cohort of PHIV+ compared with HC. Starting ART at an older age was a significant risk factor for LV hypertrophy. More advanced clinical diseases were associated with LV diastolic dysfunction.

Funding: NIH Grant 5R01HD074051, the South African Medical Research Council and AstraZeneca

Ethics: 051/2013

Title: **THE OUTCOMES OF CHILDREN WITH CEREBRAL PALSY AND UPPER AIRWAYS OBSTRUCTION AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL**

Authors: Reneva Petersen, Priscilla Springer, Kirsty Donald

Affiliation: Department of Developmental Paediatrics, Red Cross War Memorial Children's Hospital, Cape Town; Department of Developmental Paediatrics, Tygerberg Hospital, Cape Town

Background and objectives:
Children with cerebral palsy are at risk of morbidity and mortality from respiratory complications. The contribution of upper airways obstruction to respiratory problems in children with cerebral palsy is not well described. The aim of this study was to describe the prevalence and outcomes of upper airways obstruction in a cohort of children with cerebral palsy admitted over a 5 year period to a tertiary hospital in South Africa.

Methods:
A retrospective folder review was conducted of children between 2 and 18 years old who were admitted with cerebral palsy during the study period. Cases with upper airways obstruction on admission were identified from clinical notes. Information about the classification and severity of cerebral palsy, as well as investigation and management of upper airways obstruction and mortality was collected.

Results:
Three hundred and thirty children with cerebral palsy were admitted over the 5 year period. The prevalence of upper airways obstruction in the cohort during the study period was 8.8% (n=29).)The majority of children had severe spastic cerebral palsy. (Spastic tone: n=286, 87%; GMFCS IV and V= 68%, n=228)
Nineteen children were assessed to have multifactorial contributors to the upper airways obstruction (n=19). Tracheostomy tube placement was performed in nine children. In eighteen children a decision was made to offer only supportive medical management. The finding of upper airways obstruction was more likely to occur in children with epilepsy (p=0.002) and feeding complications (p=0.004) There were no predictors for death or tracheostomy tube placement amongst children with upper airways obstruction.

Conclusion/ Significance:
This report highlights the multifactorial causes of upper airways obstruction and vulnerability to respiratory compromise and mortality in children with severe cerebral palsy who have this problem. While tracheostomy tube placement is used internationally and locally as definitive airway management in children with cerebral palsy with UAO, information about the quality of life of affected children and caregivers is lacking especially in resource limited settings. Further research into this important clinical problem is indicated.

HREC/REF: 916/2014

Title: **SNP ARRAY ANALYSIS IN CNV DETECTION: A STUDY TO ASSESS THE FEASIBILITY OF INTRODUCING DIAGNOSTIC TESTING**

Authors: T Ruppelt, K Fieggen, R Ramesar

Background:
Intellectual disability/developmental delay (ID/DD) is a significant problem in child health affecting 2 to 3% of the population worldwide. While the underlying aetiology of ID/DD is not always known, up to 20% of cases may be due to chromosomal imbalances detectable by microarray analysis.

Methodology:
The Affymetrix® Cytoscan™ High Density (HD) Array containing over 2.4 million markers for copy number (CN) was used to detect genome-wide high resolution CN and single nucleotide polymorphisms (SNPs) in a cohort of 27 carefully selected patient samples.

Results:
Seven of the patients (26%) demonstrated pathogenic copy number variants (CNVs). Diagnoses included well-described genetic syndromes as well as a susceptibility locus for neurodevelopmental disorders. Three variants of unknown significance (VOUS) were detected.

Conclusion:
The results obtained in this study confirmed the superiority of SNP based array technology in the detection rate of CNVs in patients with ID/DD over conventional karyotyping. Clinical utility is confirmed in a South African population and facilitated establishment of a diagnostic service.

Title: **PAEDIATRIC RHEUMATOLOGY ACCESS IN THE DEVELOPING WORLD – THE IMPACT OF GEOGRAPHIC HOUSEHOLD LOCATION ON CHRONIC PAEDIATRIC RHEUMATOLOGY FOLLOW UP CARE**

Authors: Waheba Slamang and Chris Scott

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Background
Children with chronic illnesses are particularly dependent on appropriate referrals, to access specialist and subspecialist health care for diagnosis, optimum treatment and better outcomes. Distance from health care services, cost, household income and transportation are often described as barriers to health care access. Awareness of these factors should inform the planning of chronic follow up care

Objective
To map the geographic household locations of patients referred to the paediatric rheumatology (PR) service in Cape Town 2010- 2015 and analyze the distances travelled for follow up care

Methods
A retrospective, systematic review of all patients attending the PR service between 1 January 2010 to 31 December 2015 was performed.
Patients requiring follow up were identified from medical records and further grouped as actual clinic attenders or non-attenders.
Household locations were mapped and driving distances to the clinics attended calculated, using Google maps. Travel times were not considered, due to lack of retrospective information on variations in access to transportation.
Statistical analysis of driving distances for attenders and non-attenders were considered significant if $p < 0.05$

Results
533 patients were seen at the Cape Town PR service. Referrals from the City of Cape Town Municipality in the Western Cape, comprised the majority 471 (88.4%)
Of the total number of referrals, 326 were identified as requiring follow up care and fulfilled inclusion criteria. 196 (61.1%) patients, 60 males and 136 females, with a median age 108 months, arrived for follow up care and were classified as attenders. 126 (38.9%) patients, 56 males, 70 females, with a median age of 103.2 months, did not arrive for follow up care and were classified as non-attenders.
Chronic attenders travelled a median distance of 18.76km (IQR 11.42- 26.8km)
Non-attenders travelled a median distance of 16.65km (IQR 10.8- 24.5km)
There appears to be a negative correlation between the driving distance to the Cape Town (PR) service and overall attendance for follow up ($p= 0.013$, Odds ratio 0.996)

Conclusion
Referred patients are appropriately, predominantly from the City of Cape Town municipality in the Western Cape. This includes the main health services drainage areas in the Western Cape for the tertiary hospitals where the paediatric rheumatology service is located.
In this cohort of patients, distance per se appeared to have a negative correlation with clinic attendance.
Further investigation into additional factors affecting follow up clinic attendance is warranted.

Title: **PARTNERSHIPS FOR CONGENITAL HEART DISEASE IN AFRICA (THE PROTEA STUDY) - A CHD COHORT FOR AETIOLOGICAL, INTERVENTION AND OUTCOME STUDIES**

Authors: Inge Smit[1], Susan Perkins [1]Bernard Keavney[2], Alistair Revell[3], Rik De Decker[1], John Lawrenson[1,4], George Comitis[1], Barend Fourie [4], Lenise Swanson[1], Blanche Cupido[5], Gasnat Shaboodien[6], Rajkumar Ramesar[7], Bongani Mayosi[8], Liesl Zühlke[1, 5]

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Background:
Congenital heart disease (CHD) is the most common birth defect world-wide, affecting 8/1000 live births. CHD has additional public health implications in low and middle-income countries. Yet, the reported prevalence of CHD in Africa is significantly lower than in developed economies, likely reflecting missed diagnoses and the poor early prognosis of serious lesions in resource-limited environments. We thus aim to address the current gaps in evidence in CHD epidemiology in our context.

Objectives:
The three main objectives of the study are to establish a comprehensive phenotype and genotype registry, to develop a biobank for DNA extraction and genetic analysis; and to utilise computational fluid dynamics to potentially develop new treatment modalities for CHD.

Method:
The Partnerships in Congenital Heart Disease in Africa (PROTEA) study is a prospective, hospital-based registry that has been established at the University of Cape Town. This two-year study will enroll 1200 participants from three tertiary hospitals: Tygerberg, Groote Schuur and Red Cross War Memorial Children's Hospitals following funding from MRC-UK and with collaboration between several partners and institutions.

Conclusion:
We present the PROTEA Study, a comprehensive data collection effort for CHD patients throughout the life course. We anticipate that this could provide a platform for further research and collaborative partnerships in South Africa and African institutions. Our study will provide an Africa-specific evidence base and record of phenotypic / genetic characteristics of CHD and provide comprehensive, contemporary data on patients with CHD. Finally, we believe that these data will add significantly in the development of strategies to prevent and manage CHD in the African context.

Title: **A PROTOCOL FOR A SYSTEMATIC REVIEW OF THE DIAGNOSTIC ACCURACY OF HAND-HELD ECHOCARDIOGRAPHY FOR THE DETECTION OF RHEUMATIC HEART DISEASE IN SCHOOL-AGED CHILDREN AND ADOLESCENTS**

Authors: Lisa Telford[1], Liesl Zühlke[2], Eleanor Ochodo[3], Mark Engel[1]

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Background/Objective:
Rheumatic heart disease (RHD) is an easily preventable and treatable chronic condition which continues to persist in many developing countries largely affecting impoverished populations. Handheld echocardiography presents an opportunity to address the need for more cost-effective methods of diagnosing RHD in developing countries, where the disease continues to carry high rates of morbidity and mortality. Preliminary studies have demonstrated moderate sensitivity as well as high specificity and diagnostic odds for detecting RHD in asymptomatic patients. We describe a protocol for the systematic review of published primary diagnostic test accuracy studies to evaluate the evidence for this portable technology in diagnosing suspected RHD.

Methods/Design:
Electronic databases including PubMed, Scopus, ISI Web of Science and EbscoHost as well as reference lists and citations of relevant articles will be searched using a predefined strategy. Primary observational studies which evaluate the diagnostic accuracy of hand-held echocardiography compared to standard echocardiography will be selected. The methodological validity and quality of studies deemed eligible for inclusion will be assessed against review specific QUADAS-2 criteria and information on metrics of diagnostic accuracy and demographics will be extracted by two reviewers independently. Forest plots of sensitivity and specificity as well as a scatter plot in Receiver Operating Characteristic (ROC) space will be used to investigate heterogeneity. If possible, a meta-analysis will be conducted to produce summary results of sensitivity and specificity using the Hierarchical Summary Receiver Operating Characteristic (HSROC) method. In addition a sensitivity analysis will be conducted to investigate the effect of studies with a high risk of bias.

Conclusion/Dissemination:
The planned review will provide a summary of the diagnostic accuracy of handheld echocardiography. Results may feed into evidence-based guidelines and should the findings of this review warrant a change in clinical practice, a one-page summary report will be disseminated among leading clinicians and healthcare professionals in the field. This review protocol is registered on the PROSPERO international prospective register of systematic reviews with the registration number CRD42016051261.

Title: **USE OF THE COMBINED SANDIFORD - ALCIAN BLUE STAIN TO DEMONSTRATE KLEBSIELLA BIOFILMS IN AUTOPSY CASES**

Authors: G. Williams, X. Mbutho, H. Buys, B. Eley, K. Pillay

Objective:
To produce a staining technique whereby gram negative bacteria may be distinguished from bacteria producing biofilms using the Sandiford's stain and Alcian blue stain at pH 2.5 in a single method.

Materials and Methods:
The histology reports and slides of 15 autopsies of children were reviewed where the cause of death was Klebsiella sepsis. Of these cases, five show exuberant bacterial colonies histologically. These cases were chosen to develop the Sandiford - Alcian blue stain.

Results:
The combination of Sandiford's stain and Alcian blue stain at pH 2.5 stained the colonies of gram negative bacteria red and highlighted the proportion of bacteria with biofilms as blue. Of the lung sections in the 5 cases, only one case showed diffuse biofilms, three showed focal biofilms and one case was negative. Three of these 5 cases had bacterial colonies in the gastrointestinal tract: One case had diffuse biofilms (focal in the lung), while the other two cases showed focal biofilms.

Conclusion:
This new dual stain can be used to highlight a high risk group with infection by Gram negative bacteria that may not respond appropriately to antibiotics due to the focal or diffuse presence of biofilms.

Title: **INSIGHTS INTO INFECTION RELATED DEATH IN INFANCY IN THE WESTERN CAPE AREA – A RETROSPECTIVE REVIEW**

Authors: Andrea L. Young, Felix S. Dube, Lorna J. Martin, Laura J. Heathfield

Objective:
A retrospective review was undertaken to provide insight into the medico-legal aspects surrounding infectious pathology in Sudden and Unexpected Death in Infancy(SUDI) cases admitted to Salt River Mortuary, Cape Town, Western Cape.

Methods:
Medico-legal case folders of SUDI cases admitted to Salt River Mortuary between 1 January 2015 and 31 December 2016 were reviewed. Clinical history, demographic information, environmental risk factors and postmortem findings were collected and recorded using Microsoft Excel 2016 (Microsoft Corporation). SPSS Version 24 (IBM Statistics) was utilized to analyze data and descriptive characteristics. (HREC Reference No.: 102/2016)

Results:
Infant death (<1 year of age) contributed a mean of 10% of all admissions to Salt River Mortuary between 2015 and 2016, with the majority (75.6%) admitted as SUDI cases. Within the SUDI group, 73.6% of cases were infection-related, and of these, 78.6% were due to respiratory-related pathology. The incidence of respiratory infection remained consistent over this two-year period. Modal month of death varied between years, May (2015) and July (2016). Notably, cause of death showed a significant association with side sleeping positon (*p=0.002)*. Cause of death was also associated with breast feeding, natural delivery in a medical center and antenatal care. SUDI cases classified as other infection cause of death (non-respiratory related infection) coincided with a 53% bottle-fed rate.

Conclusion:
From this study, it is evident that infection was the leading cause of death amongst SUDI. Although the months of highest admissions to Salt River Mortuary vary between these years, they both fall into periods of seasonal change in Cape Town. Sleeping position showed a significant association to respiratory related pathology cause of death, possibly attributed to the 'pooling' effect of mucus in the respiratory tract during sleep, similarly experienced in prone position. The second leading cause of infection was classified as other (non-respiratory related infection), which comprised 56.8% gastroenteritis cases. Within these cases, the modal choice was bottle feeding, 67%. This study highlights the importance of understanding contributory factors towards death outcome and may identify areas requiring attention to curb the devastating burden of SUDI in South Africa.

Contributions of Persons Involved:

LJH
- Conceptualization of Retrospective Review of Infection related SUDI

LJH and LJM
- Provision of SUDI database from 2015 and 2016

ALY
- Identification of Infection related cases from database provided
- Identification of factors contributing to infection related pathology (120+ variables)
- Categorization of cause of death
- Data entry from both digital and hard copy case files
- Statistical Analysis using SPSS Version 24

FSD
- Intellectual contribution for identification of risk factors and statistical analysis interpretation

NOTE**:** An abstract based on the retrospective review focusing on microbiological infection related aspects (HIV/TB incidence, exposure and symptoms) has been submitted for consideration to present at the 7th FIDSSA Conference (9 – 11 November) in Cape Town.

Title: **RETROSPECTIVE OF 2017 CARDIAC SURGERY- THE INTERNATIONAL QUALITY IMPROVEMENT COLLABORATIVE EXPERIENCE**

Authors: Liesl Zühlke,[1, 2] , Lenise Swanson [1], John Lawrenson [1,3], George Comitis [1], Barend Fourie[1,3], Rik DeDecker [1], Roxi Vergotine[4], Andre Brooks [5], John Hewitson[5]

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Introduction:
The International Quality improvement collaborative for Cardiac surgery in developing surgery (IQIC) was established to improve quality in cardiac surgery programs in developing countries. The vision of the IQIC is to facilitate a collaborative comprised of healthcare teams from around the world working to create a culture of patient safety and sustainable quality improvement infrastructures for children receiving congenital heart surgery in developing world programs. The collaborative aims to create tailored quality improvement strategies to reduce mortality and major complications for developing world programs. And to populate a database to track clinical outcomes of in-hospital and 30-day mortality, surgical site and blood stream infections, as well as other critical indicators for congenital heart surgery.

Methods:
Data from all cardiac surgery patients from 2016 is collected into a RedCap database including variables including demographics, pre-surgical morbidity, RACHS scores and 30-day mortality, with ethics approval HRECR107/2014.

Results:
A total of 166 children were operated in the first half of 2017, 8 children had two operations in this period, 3 had three operations in this six month period. The mean age was 5,33 months (SD 3.8, IQR 1-16) Of the cohort, 53% were girls. The RACHS-1 classification for severity was 24 (14.4%), 92 (55.4), 38 (22.9), 8 (3) and 3 (1.8%). There were 36 (21.6%) children with major additional chromosomal abnormalities, the most common being Trisomy 21 and 22Q Deletion syndrome. There were 14 in-hospital deaths and 2 additional deaths within the first 30-days.in-hospital mortality, 30-day outcomes and any major surgical morbidities.

Potential impact:
This is only the second African site for the IQIC. We anticipate that we will use our involvement to improve quality and consider new hypotheses and quality improvement strategies.